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ITS PREVENTION AND CURE

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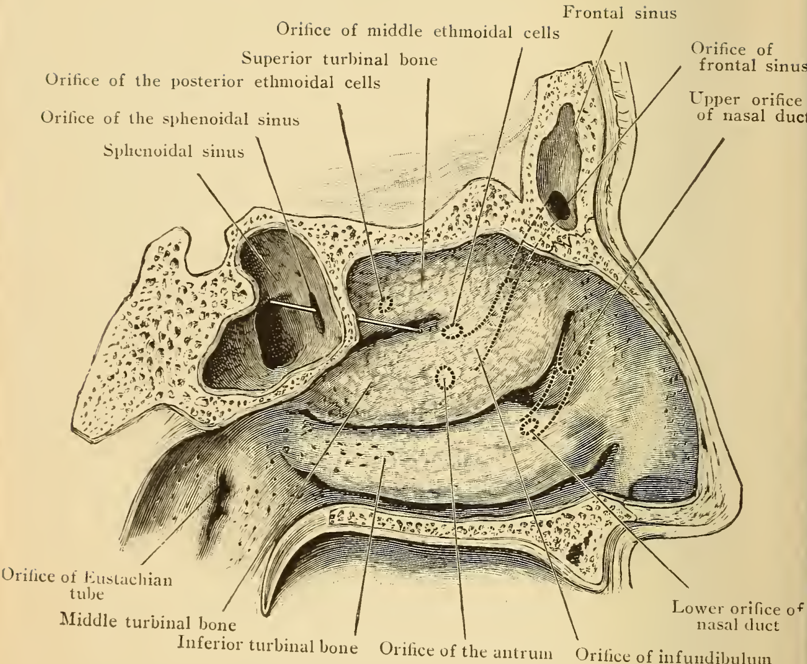

SECTION OF THE NOSE, SHOWING THE TURBINAL BONES AND MEATUSES WITH THE OPENINGS IN DOTTED OUTLINE.
(*After Morris' "Text-Book of Anatomy."*)

HAY-FEVER

ITS PREVENTION AND CURE

BY

William Clarence

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PREFACE TO THE FOURTH EDITION, REVISED

Since the last edition of my book on Hay-Fever, published six years ago, great advance has been made. The theory that pollen might be the cause has been at last demonstrated and actually proven to be a fact, and the works of Blackley, Wyman, Dunbar and Scheppegrell have at last crystallized into certainty. We now know that the emanations of vegetable matter actually cause hay-fever, that different parts of the United States produce different pollens, so the treatment of hay-fever in one portion will be different from the treatment in another. The West, North, and East, will call for a different immunizing process than that of the Middle States, yet any one can prevent his annual suffering by selecting the proper anaphylactic reaction from inhaled atmospheric pollens. While these pollens vary in different localities at various seasons, and their degree of reaction on sensitive subjects, yet the true factor can soon be found, and the un-

fortunate victim will obtain complete relief. Hay-fever is now successfully treated by immunizing the patient in advance of the attack, by the use of the same pollen that creates his trouble. The only difficulty to overcome, is to be sure to find the pollen that produces the actual mischief. This is, therefore, an individual study, not very difficult if the patient works in harmony with his physician.

As Dr. William Scheppegrell, of New Orleans, a leading authority on hay-fever and the President of the Hay-Fever Prevention Association, says: "Any physician with experience in hay-fever cases has observed the great difference in the intensity of the symptoms and in the reactions to the diagnostic tests. In some cases, the injection into the skin of five units will produce a positive, but mild and transient, reaction while in others, the same number of units will produce a wheal three centimeters in diameter and surrounded by a wide area of infection and lasting for many hours. In the former, with a low degree

of anaphylaxis, the doses may be increased with comparative rapidity and safety, and must reach a high number of units in order to be effective. In the latter, however, the increase must be made cautiously and the maximum dose carefully determined.

Another point of importance in the successful treatment of hay-fever is to remember that all hay-fever patients east of Kansas are not necessarily victims of the *Ambrosiacae* (Ragweed) group; or, even if this is the case, that this is not the only cause. In a large area of the Northeastern States, for instance, the Russian thistle, *Salsola pestifer,* is a potential cause of hay-fever infestation, that should be carefully considered in the successful treatment of these cases. This is especially important, as these cases do not respond to the diagnostic tests of the *Ambrosiacae* group and are not benefited by the injection of these pollen extracts.

If the "extensive" methods of treatment are followed, in which no diagnostic

tests are made and no cognizance taken of the varying degree of sensitivity and the different kinds of pollen involved, the result will be disappointing to the patient and an apparent reflection on the immunizing method. The "intensive method," however, in which all the factors bearing on each individual case are carefully considered, will not only give satisfactory results to the patient and physician, but will place this method on the scientific basis to which it is entitled.

Some manufacturers of pollen extracts, not taking cognizance of these factors, have attempted to simplify the immunizing method by preparing mixtures containing the most common pollens. Many of these contain not only pollens responsible for hay-fever, but even some that, for various reasons, the patient never has an opportunity to inhale. The result of this "shotgun" method is that the patient usually receives an injection containing a mass of inert protein that leaves the possibility of benefit very doubtful.

It has been estimated that in New England and the Middle States, 90 per cent. of the June hay-fever (rose cold) comes from timothy grass and same percentage of the July and August hay-fever from ragweed. If this is true, then we have a safe working basis, for our patients will tell us how and when they receive their infection. While we have found hay-fever is caused by the pollens of certain plants, yet for many years we did not know that it was excited by wind pollinated plants and not by the insect pollinated. This is an important fact to be remembered as insect pollinated plants contain a noxious element and will give a positive skin test in certain individuals. For many years the medical profession drifted away from the local applications of remedies, even for the relief of hay-fever. I have invariably found much comfort and satisfaction in local treatment, and many of my patients insist on having it. Dr. G. M. Mackenzie, of New York, is favorably imprest with specific local applications. His conclu-

sions are as follows: (1) The reactivity of the nasal mucosa of hay-fever patients may be markedly diminished by spraying the nose and throat with the specific pollen antigen. (2) In a series of patients (38) given specific prophylactic treatment by this method the results compared favorably with those in a series of patients treated by specific subcutaneous injections, but were less satisfactory than when a combination of the two methods was employed.

I am giving the article of Dr. I. Chandler Walker, of Boston, Mass., "The Frequent Causes and the Treatment of Hay-Fever," in full, so the reader may study his personal technic.

W. C. Hollopeter.

Philadelphia, March, 1922.

PREFACE TO THE FIRST EDITION

Having had remarkable and uniform success with a simple treatment of hay-fever for the last twenty years, during which time I have given complete relief to many patients in my private practise, and having made a thorough clinical study of this affection, as well as an exhaustive review of the literature relative to it, I feel justified in presenting the results of my labors in this short treatise.

There is little to be said definitely about the etiology of the disease. It is undoubtedly caused by an external irritant, possibly containing a micro-organism or a toxin, which becomes especially active in the nasal passages of an individual predisposed by systemic debility or local

abnormality. We acknowledge the element of neurotic disturbance, but to dogmatically define its exact cause and *modus operandi* is beyond us.

In order that the best thought of the subject may be presented to the reader, I have compiled, arranged, and annotated the most worthy literature, and I acknowledge my indebtedness to the many writers quoted. The most of my original communication is devoted to the all-important point in the discussion—the successful treatment. A complete bibliography is appended.

W. C. HOLLOPETER.

INTRODUCTION

Next to tuberculosis, hay-fever is one of the most interesting and common diseases, and has received an enormous amount of study. While it is not directly fatal, it is exceedingly distressing and is certain by its annual visitation to lower the vital resistance and induce other illness in the body. In this way it becomes a prolonged and serious menace to the comfort and happiness of the sufferer. Hay-fever was not regarded frequent in the young until a more careful study of autumnal and spring catarrhs among neurotic children revealed the fact that the same troublesome complaint had occurred the previous season. The frequency of "cold taking" among children is due to their lowered vitality, the result being

adenoids and enlarged tonsils which often precede the typical hay-fever.

It has been found that children, especially the neurotic offspring of nervous parents, are as subject to hay-fever as adults, if not more so, for we certainly have an ever-enlarging army of catarrhal children. There is no doubt that in every class hay-fever is decidedly on the increase in America. True hay-fever is also found in great masses of thoughtful adults, who are prone to forget the previous attacks, altho they may have had many annual visitations of the disorder. Some slight exposure, or irregularity of diet, or an unusual change in the atmosphere, suffices to explain the indisposition, and satisfies the mind for the time. It is certain that a large number of hay-fever sufferers forget from year to year the annual visitation; this is more likely if the attack has not been severe. Furthermore, it has been

most conclusively proved by many authorities that hay-fever does not occur unless we have a conjunction of three necessary factors:

1. An external air-borne irritant.

2. A sensitive or diseased nasal mucous membrane.

3. An unstable nerve-center.

Upon the simultaneous manifestation of these three factors in any individual we are reasonably sure in making a diagnosis of hay-fever. An absence of any one of the three admits at once of distinct doubt.

The claim for originality in this thesis lies in the fact that the author recognizes the three essential factors, as stated above, as the cause of hay-fever, and claiming that the remedy lies in controlling or destroying the habit, by inhibiting or benumbing the sensitive nasal surface by local cleansing and massage. The literature of hay-fever has grown so very pro-

lifically in the last five years that to follow it out in detail would be a difficult and useless task. Most writers agree as to the three essential causative factors, and volumes have been written in discussion of their different phases.

Dr. Geo. M. Beard, one of the earlier and most exhaustive writers, regards it as a neurosis, due to an unstable brain-center, and a functional disease of the nervous system, thus ignoring all environment, climate and nasal conditions. Sajous, on the other hand, regards the trouble as one of local origin, ignoring heredity and neurosis, and finds an abnormal nasal chamber in all active cases. They both concede external irritants as essentially necessary to the initial paroxysm, but regard this of secondary importance. It was not until Prof. Dunbar and his followers made their exhaustive studies of pollen that we arrived at any satisfactory scientific knowl-

edge as to the exact nature of this "external irritant," and applied the antidote for its control. Literature on hay-fever during the past ten years has centered largely on discussion of these studies. It is for this reason that I have given Dunbar so large a space in my book. I have allowed him to speak for himself.

In my first published paper in 1898, I stated that I had succeeded in controlling a large number of cases by "scrubbing most carefully every portion of the mucous membrane of the nasal chamber, being sure to reach between the turbinated bones and all around any slight prominence." Musser and Kelly ("Practical Treatment," 1913, Saunders, Philadelphia) quote E. W. Wright as placing great stress upon the hypersensitive condition of the nasal mucosa as the important causative factor in many cases, suggesting a frictional massage of the mucous

membrane of the nose in order to increase its resisting powers, so that it can withstand the irritation and excitation from the impact of the pollen of plants. His method is to apply gentle massage to the nasal mucous membrane through the medium of a cotton-covered probe. These applications are to be made daily for from three to five minutes in each nasal chamber.

I am unable to find any additional authority for this method of management of the disease. The observation of Wright was made long after the publication of my paper; and certainly priority for such local treatment belongs to me.

PART I

WHAT HAY-FEVER IS

HISTORY, PERIODICITY, SYMPTOMS AND DIAGNOSIS

PART I

WHAT HAY-FEVER IS

HISTORY, PERIODICITY, SYMPTOMS AND DIAGNOSIS

1. Definition, History and Bibliography

Among the synonyms that have been employed for the term hay-fever may be named the following: Autumnal catarrh, Bostock's catarrh, coryza vasomotoria, coryza vasomotoria periodica, hay-asthma, idiosyncratic coryza, June cold, July cold, nervous coryza, nervous catarrh, paroxysmal sneezing, peach cold, periodic hyperesthetic rhinitis, pollen catarrh, pollen poisoning, pruritic catarrh, pruritic rhinitis, ragweed fever, rhinitis sympathetica, rhinitis vasomotoria, rose catarrh, rose

cold, summer bronchitis, summer catarrh, summer catarrh from idiosyncrasy, summer fever, typical early summer catarrh, vasomotor coryza, vasomotor rhinitis. In other language are the following equivalents: *Latin*—Catarrhus æstivus, coryza vasomotoria periodica; *French*—Catarrhe d'été, catarrhe de foin; *German*—Frühsommerkatarrh, Heuasthma, Heufieber; *Italian*—Asma dei mietitori, febbre del fieno, asma del fieno.

The term "hay-fever" was first used to designate the form of disease occurring in the autumn in distinction from like affections which occur in other seasons. So universal, however, has become its use that it is now employed to designate all the forms of what may be called the periodic influenzas, irrespective of seasons.

Hay-fever may be defined as an affection of the upper air-passages occurring

periodically, usually at or near a fixt date in the early autumn, sometimes in the spring or summer, characterized by its sudden onset and as sudden termination in certain atmospheric conditions, by swelling and turgescence of mucous membranes of the nasal fossæ and adjacent cavities, irritating discharges therefrom, and various symptoms of coryza, and occasionally by asthmatic paroxysms. It always results from the combination of a special predisposition, from depraved resistance or lowered vitality of the general system or a local lesion, and an exciting cause, believed to be a micro-organism or peculiar toxin, generally arising from pollen or dust deposited upon or in the mucous membrane of the upper air-passages. The important predisposing causes are: heredity, idiosyncrasy, neurotic temperament, peculiar susceptibility of the vasomotor

system, generally debilitated condition, deranged assimilation, and a local lesion. Hay-fever has been defined as a neurosis, as an idiosyncrasy, as a catarrhal affection, and as a type of influenza, and as various combinations of these. The deposition of some special irritant is universally regarded as the exciting cause.

Exactly when hay-fever was recognized as a distinct affection is not known. Beschorner shows that it was known in the sixteenth century. In 1565 Botallus reported a case. Van Helmont and Binninger, in the seventeenth century, speak of it. A similar distressing catarrhal affection, but due to the rose, is instanced in "Acta nat. curios. Ephemerides," Dec. II, Ann. V, obs. 22, and again in the same journal, Dec. III, Ann. V and VI, obs. 193, a case of annually recurring profuse nasal catarrh is mentioned. John Floyer,

London, 1698, noticed that there were peculiar cases of asthma in which the attacks were longer and more acute in summer than in winter. In Good's "Study of Medicine" there is a reference to a case related by Timæus in 1667, of an attack of an asthmatic nature caused by the odor of roses and ipecac. Riedlin, in his "Lin. Med.," p. 177, in 1695, wrote of the odor of roses causing a catarrh of the head, resembling hay-fever. C. L. Parry, of London, records a case in 1809 and another in 1811. Elliotson, in 1821, tells of a patient who had had hay-fever since 1789, and of another who was sixty-six years of age and who had had the disease from his seventh year, *i.e.*, since 1755, and of a third who had been afflicted for many years.

Just when and where the term "hay-fever" or "hay-asthma" arose it is im-

possible to say, but probably it was popularly so named. The emanations from dry hay were first thought to have caused it. Dr. Bostock, who was himself a sufferer, in 1819, found that the laity knew of the affection, altho it was not recognized as a distinct disease by the profession. He objected to the term "hay-fever," which was already employed to designate it in his day, contending that moist heat, sunshine, dust, and fatigue were more potent in its causation than emanations from dry hay. It seems remarkable that the profession in England were unfamiliar with hay-fever as a distinct affliction, especially as their king, George IV, was a sufferer from it. In 1828, Bostock, who had first described the disease to the Medico-Chirurgical Society of London as a "case of a periodic affection of the eyes and chest," published some further ob-

servations on the complaint under the title "Summer Catarrh," or "Catarrhus Æstivus." In 1828, MacCulloch included it in his "An Essay on the Remittent and Intermittent Diseases," but advanced no special views. In 1830, Augustus Prater published notes of a case seen in Paris. In 1831, Dr. Elliotson, in London, briefly described the affection; and in 1833 he discust the complaint more fully and opposed Bostock's theory of heat and rejected the hay-theory of its origin, but declared grasses to be more important factors; and he first pointed to pollen as the probable cause of the disease. In 1847, Dr. Ramadge detailed reports of cases and believed "effluvia from flowers" caused it. In 1850, Gream first alluded to dust as an exciting cause and proposed nux vomica as a remedy. In 1852 Dr. Laforgue, of Toulouse, wrote his essay "Observation

de catarrhe d'été,'' in which he upheld heat as the cause, after the view of Bostock. But in the next year, 1853, in "L'Abeille Médicale,'' an anonymous contributor, reciting his own case, advocated hay-emanations and not heat as the exciting agent. In 1854 Phœbus, of Giessen, concluded from his study of 154 cases that sunlight was the active cause of the attacks. In 1857 Watson ascribed the malady to the presence of vegetable matter in the atmosphere. In 1859 Phœbus again published the results of his circular of inquiry. He went into the subject more thoroughly than any of his predecessors, and from sunlight he shifted to ozone as the theoretic cause of the malady. In this same year Hyde Salter named as the exciting agents "bright, hot, dusty sunshine,'' a full meal, and hay, and recited two interesting cases. Another writer,

Walshe, in the same year, referred to hay-fever as a singular variety of nasopulmonary catarrh, and he first called attention to the fact that the disease, in his own person, "always disappeared in crossing the Atlantic."

In July, 1860, Dr. Cornaz, of Neufchâtel, Switzerland, in a paper on hay-fever, described six cases, and concluded that the flowers of grasses were the cause of the disease, and he was followed on the 20th of August of the same year by Dr. Labosse, of Nitry, France, in a paper entitled "Nouvelle observation de catarrhe de foin," in which he spoke of three persons whose symptoms occurred at the time certain flowers were in bloom. In 1866 strong light and great heat were advanced as aggravating causes by Dr. Wm. Abbotts Smith. In his published work, "On Hay-fever, Hay-asthma, or Summer Ca-

tarrh," he rejected the ozone theory of Phœbus.

In 1867 the nervous origin of the disease was first advanced by Dr. William Pirrie, who spoke of two forms,—one a spasmodic form caused by external irritants, the other arising from the action of light and heat upon the central nervous, the cerebrospinal, and sympathetic systems. In the same year, Helmholtz, who, tho not a general practitioner, while suffering from hay-fever, began to treat it with a quinin solution and found that he was relieved thereby. Two years later he detailed to C. Binz, of Bonn, Germany, by letter, the history of his sufferings, and recommending his solution as a ready means of relief and even of prevention, which was in accord with the findings of Binz that the quinin solution was poisonous to infusoria. In this letter Helmholtz

propounded the theory that the symptoms were caused by vibrios which, tho latent at other times in the nasal fossæ and sinuses, were excited to activity by the heat of summer. It has since been thought that the organisms found by Helmholtz, by means of the microscope, in the nasal discharges during an attack were probably fragments of mycelium-like threads which develop from pollen-cells under the influence of the heat and moisture of the nasal chambers and which contain the minute fovilla of the pollen-cells. The use of the quinin solution which Helmholtz so successfully employed on himself became very popular and found many strong advocates in the profession until the extensive researches of Blackley in regard to pollen in 1873. In the meantime, in 1870, Dr. George Moore advocated a complex theory of the disease, really com-

binations of preceding theories. In the same year Roberts issued a short, practical paper, claiming to be the first to observe excessive coldness of the tip of the nose as the "pathognomonic" symptom of hay-fever and desiring credit to be accorded him for this discovery.

In 1872, Morrill Wyman, of Cambridge, Mass., distinguished two different forms of the disease; naming that occurring in August "autumnal catarrh," peculiar to America, and that of the spring or early summer "June cold" or "rose-cold," more prevalent in England.

Dr. Wyman first attempted to define the geographical limits of the disease, and called attention to the important fact that residence in certain elevated regions brought certain and complete relief in most cases of autumnal catarrh. He stated that a lady from Lynn, Mass., a

great sufferer, accidentally observed in 1853 that her catarrh passed by while she was traveling in the White Mountains, and that for the following ten years she visited the region and escaped the disease. In 1860, Jacob Horton, of Newburyport, Mass., wrote Dr. Wyman that the White Mountains gave the only relief. In 1873, Charles H. Blackley, of Manchester, endeavored to show that pollen mainly, if not exclusively, caused the malady, and by extensive experiments showed that the amount of pollen in the atmosphere at great elevations was to that in the air at ordinary breathing levels as nineteen to one. He proved, by very ingenious and carefully conducted series of experiments, that the pollen of grasses and flowers was the sole cause of hay-fever in himself, and that in two other patients the severity of the attacks was directly related to the

amount of pollen in the air. His subsequent observations made it extremely probable that pollen is an important factor in the causation of hay-fever, altho all kinds of dust may be sufficiently irritating to excite the paroxysms. This was in opposition to the views of Phœbus and of Pirrie, both of whom suggested heat, strong light, and ozone as the exciting causes. Pirrie had also suggested disturbance of the central nervous system as an important etiologic factor. He was supported in this view in 1876 by Morrill Wyman, then of New York. In the same year Beard, of New York, published his monograph, the information for which had been painstakingly gathered from replies to two hundred circulars which he had issued to medical men all over America, somewhat after the manner of Phœbus; altho, unlike Phœbus, Beard had himself

seen and treated many cases. From his data he drew the conclusion that the immediate exciting causes were more than thirty in number, and that secondary causes might increase this list to more than one hundred. He showed also from his statistics that the nervous temperament existed in a great proportion of the sufferers, and that nerve tonics were of some value. In 1877, Marsh, of Tuckerton, New Jersey, published an essay in which he accepted completely the pollen theory. He first called attention, in this paper, to the activity of the pollen of *Ambrosia artemisiæfolia,* or common ragweed, as by far the most active of the pollens in America in producing the attacks.

In 1882, Daly, of Pittsburgh, first called attention to the fact that a diseased condition of the nasal cavities was an important factor in the production of the exacer-

bations of the disease. Roe, of Rochester, in 1883, advocated the same theory, but added that "removal of the diseased tissue removes susceptibility to future attacks." In the same year, Sajous' essay appeared in which he advanced idiosyncrasy as a heretofore unconsidered element in the cause of hay-fever, and laid stress upon the three essential factors in the production of an attack; viz., first, an external irritant, second, a predisposition of the system, and, third, a vulnerable or sensitive area. In 1883, Hack accepted the local theory of the causation of the disease. In 1884, Harrison Allen, of Philadelphia, attributed the affection to a permanent or temporary obstruction of one or both nasal chambers. In the same year, J. N. Mackenzie, of Baltimore, termed the disease "coryza vasomotoria periodica," because it is essentially a coryza. He

says: "The well-recognized, but imperfectly understood personal susceptibility to certain forms of local irritation, which is the sad prerogative of sufferers from this disease, has always been the stumbling-block in its investigation and the rock upon which the various speculations as to its nature have been wrecked." He demonstrated that "there exists in the nose a well-defined sensitive area whose stimulation, through a pathologic process or through *ab extra* irritation, is capable of producing an excitation which finds its expression in a reflex act or in a series of reflected phenomena." He thus claimed functional derangement of nerve-centers as essential to the disease. It was also in 1884 that Sir Morell Mackenzie asserted that the universal cause of the disease was pollen, altho he did not deny that other irritating particles, *e.g.*, ipecac, if per-

sistently brought in contact with the mucous membrane of the nasal chambers, may produce it.

In 1885 Seth S. Bishop advocated the uric acid theory of the origin of the disease.

In 1887 Sir Andrew Clark, in the Cavendish Lecture in London, emphasized the doctrine of the three great causative factors,—viz., first an exciting agent, generally pollen; second, the neurotic habit; and, third, a local morbid condition of the nasal mucous membrane.

Since then many articles have appeared upon the subject, but no striking innovations in the possible etiology of hay-fever have been offered.

In 1893, Macdonald said, we ought not to describe hay-fever as a disease but merely as a train of symptoms—a train of physiologic reflexes instigated by an

unwarrantably small provocation in certain individuals more susceptible to the influence thereof than the rest of their kind.

Early in 1897, Grayson, of Philadelphia, stated that "the neurotic habit may exist but is not essential to the disease, and the nervous system is implicated as a victim, not as a culprit." He claimed that hay-fever is a defect, not of the nervous, but of the nutritive system, believing that the digestive tract is the cradle of the systemic error.

In October, 1897, Edmund W. Holmes, of Philadelphia, stated his belief to be that hay-fever was largely a neurosis, originating in local disease of the nasopharynx, the characteristic manifestations being in part direct, the result of central nervous modifications, and in part reflex, from the action of various mechanical ir-

ritants, aided by local and constitutional factors when they exist, and by seasonable and climatic influences, the periodic and peripheric susceptibility being in particular expressions of certain impressions.

2. Causes

The idea of an external irritant in hay-fever pervades most views of it. There can be no doubt, however, that there is usually an underlying systemic condition which renders individuals susceptible to the disease. It may, in addition, be accepted as conclusive that the nasal abnormalities found in hay-fever subjects are as often incidental as causative. They are seldom exclusively provocative of the susceptibility, and they are not the results of repeated attacks. Exactly what this underlying condition of susceptibility is has been variously regarded. The nature

of the irritant has been widely and scientifically investigated. While all theories advanced are in part more or less tenable, none of them alone is satisfactory. The condition is always, however, one of *lowered resistance,* general or local. If general, it may be of neurotic, lithemic, idiosyncratic, gastric, intestinal, or diathetic origin. It is, therefore, my belief, that in hay-fever there is always, first, an exciting agent, and, second, a system predisposed by debility of some character to the influence of this irritant. The overwhelming testimony as to the character of this irritant points to its derivation from something external to the body of the sufferer. Moreover, it is absolutely certain that without the action of an external irritant genuine hay-fever does not occur. The elaborate and ingenious experiments of Blackley, not only upon himself but upon

other individuals, clearly indicated the pollen of flowering plants as an active, exciting cause. It has never been shown that, altho pollen, healthy or unhealthy, may be a mechanical irritant and thus account for many cases, it is not also a chemic irritant when it has fallen upon a susceptible soil. It has been claimed that hay-fever is caused by a toxin generated by a fermentative process in the pollen which has fallen into the alkaline solution of the nose; and it has been shown that acid solutions stop the movements of many micro-organisms and spermatozoa, and that alkaline solutions in the nares have given little or no benefit in attacks of hay-fever. It has also been shown that the affection is more common among men than among women, and that the blood of the latter is the less alkaline.

Arnold, in 1896, stated that just what constitutes the irritant is not determined, and said it is likely that not healthy pollen but some fungoid growth is responsible, since threshers of grain, at other times without ill-effects, have complained of attacks of hay-fever after threshing smutty or moldy grain, especially oats.

Helmholtz, himself a sufferer from hay-fever, discovered peculiar micro-organisms in his nasal discharges. These vibrios were never found by others, and this fact is supposed to controvert his theory. It has not been shown conclusively that they have been sought for by other investigators, and it is likely that they have not, since attention has been called away by the pollen and other theories. The antiseptic quinin solution employed by Helmholtz, while extensively used with good results for the subsequent decade,

was not invariably accompanied by relief. Later, the relief that was given by quinin solutions was said to be psychic. This allegation may well be understood when it is considered that many other theories as to the causation of hay-fever, particularly the pollen, abounded soon after Helmholtz's expositions.

Some very interesting investigations by Strangways, of St. Louis, in 1897, urged him to conclude the amount of pollen in the air is altogether too small to have an injurious mechanical, medicinal, or poisonous influence. He calculates that for every square foot of surface there is one ragweed, and inquiry showed that mere elevation of several hundred feet above the earth's surface does not give relief from this distressing affection. Strangways found that ragweed pollen probably floats to 1,000 feet elevation; but, if the

limit is placed at 500 feet, it would give for every plant 500,000 cubic feet of air, not for one day but for six weeks; *i.e.*, if the whole plant was pollen there would be still only one part of pollen to fifteen or twenty billion parts of air. The rose and the goldenrod are in even smaller quantities. Strangways' estimates showed that there was not more than one grain of pollen for every thirty respirations. He advanced the theory that, while pollen plays a part, it does not irritate mucous membrane nor produce vasomotor paresis by its direct influence, but that a protoplasmic substance found in pollen and in the vegetable kingdom, acting as a ferment, causes the formation of a toxin which is the real exciting cause.

There can be little doubt that the neurotic element has been present in many, if not most, cases of hay-fever, and evi-

denced by depression, general lowering of tone, or exhaustion of the nervous system. The neurosis need not be acquired; in fact, it is often hereditary, which will be discust later.

Holmes believes the disease to be in great part a neurosis with other debilitating conditions. The fact that the better educated classes are most prone to this affection indicates the influence of neurotic tendency as well as exhaustion of the nervous system or debility or depression thereof. The premonitory symptoms of this affection, as ably shown by Sajous, show the neurotic elements. He well asks, "If the local irritant is the only cause, why does the respiratory tract, the portion of the body first and most exposed to its effects, not become immediately influenced?" This author also shows a case following enteric fever, the debilita-

ting and exhaustive character of which is well known, one preceded by malarial fever and another by bronchitis, pertussis, and varicella.

Of the various other theories advanced are the lithemic, the intestinal or gastric, due to lack of proper assimilation, and the uric acid diathesis. The views herein advanced are not at all inconsistent with the idea that the diatheses exercise a predisposing influence in producing the affection, which influence is debilitating and devitalizing.

The local theory alone is not conclusive nor satisfactory; viz., that the disease is due to chronic nasal catarrh, or a local lesion, upon which the exciting cause acts. There is no doubt that diseased areas are more sensitive to the irritant, and especially so in cases of lowered vital energy and lessened normal resistance, general or

local; but a large number of cases show no local disease.

In all of the theories respecting this affection there is more or less regard for the agency of pollen in provoking the paroxysms of the disease; but as every one is exposed to the irritant, in those affected the soil must be prepared for the seed, that is, before the deposition of the pollen or dust or exciting agent there must be a morbid condition preexisting, which can so far be characterized as to call it lowered vitality or general or local resistance, which springs from a variety of causes.

3. Periodicity

On the continent of Europe, where it is less frequent, and in England, hay-fever prevails in June and July. The initial attacks occur during May and June and seldom last longer than September.

In India the malady chiefly occurs in February. In Australia, in and around Adelaide, where the disease prevails, it occurs chiefly in September during the time of the blossoming of the Cape weed. In his work on hay-fever, Beard essays to show how the autumnal form is peculiar to the United States. One cause seems to be the flowering of the Roman wormweed and the pollen of corn about the middle of August, and another in the prevalence of the "dog-days." A third reason lies in the fact that there is less atmospheric ozone and electricity at this period than at any other time of the year, and, again, the hottest days are frequently in the latter part of June. Beard also attached importance to a variety of hay-fever in which the attacks came on in September. This distinction is probably due to the fact that while one person is liable to the

action of one pollen, another may be affected by a totally different pollen, and the annual attacks come on when the atmosphere is permeated by a special pollen to which the victim is individually susceptible. Many persons are susceptible to the action of more than one pollen. Patients often suffer from rose-colds in early summer, and, again, in August, from the autumnal form of hay-fever. Of the 198 cases collected by Beard the onset of the disease occurred—

From	May	1	to	May	10,	in	2	cases.
"	"	10	"	"	31,	"	6	"
"	June	1	"	June	10,	"	11	"
"	"	10	"	"	30,	"	8	"
"	July	1	"	July	10,	"	6	"
"	"	10	"	"	20,	"	6	"
"	"	20	"	"	31,	"	7	"
"	Aug.	1	"	Aug.	10,	"	7	"
"	"	10	"	"	20,	"	81	"
"	"	20	"	"	31,	"	54	"
"	Sept.	1	"	Sept	10,	"	7	"
"	"	10	"	"	20,	"	1	case.
"	"	20	"	"	30,	"	2	cases.

Of Bosworth's eighty cases the greatest number, fifty-one, occurred between August 10th and August 27th. The usual date assigned for the commencement of paroxysms of hay-fever is the 29th of August. This form of the disease, commencing in the latter part of August, is designated as autumnal catarrh.

Many patients have asserted that they are attacked annually on exactly the same date, and even the same time of day, each year. There can be little doubt that the psychic influence or peculiar mental anticipation may have a great deal to do with this circumstance. An attack may be brought on by the influence of the imagination. Phœbus gives the history of a case in which attacks of sneezing were brought on "while looking at a beautiful picture of a hay-field." The well-known instance of J. N. Mackenzie, in which an

attack of hay-fever was brought on in a susceptible individual subject to rose-cold by means of an artificial rose may be explained on this ground. Bosworth considers that the time of occurrence is influenced by psychic causes, and is analogous to the recurrence of chills in intermittent fever, and considers that deception as to the actual time of occurrence might be proved in hay-fever as in intermittent fever, in which changing the hands of the clock may lead to a change in the regular recurrence of the chills. Prince gives the history of a case in which a hay-fever subject under the influence of auto-suggestion, by means of writing frequently on paper and thinking, day and night, in leisure moments, and of slight hypnotism, prevented the premonitory symptoms of hay-fever, and she was free from the annual attacks for several years,

when they recurred and continued yearly thereafter. Prince asks, may it not be that the reason why certain places, such as Dublin, for instance, are reputed to have a specific influence against attacks, is the counter-suggestion thereby given that the patient will be free from attacks at such places?

Pirrie states that it is next to impossible to definitely decide the duration of hay-fever attacks, as seasons, age, temperament, locality, treatment, and other circumstances tend to cause variations in different years and in different individuals. Treatment will do much to curtail the duration of the more prominent and distressing symptoms, but if left to themselves it is seldom they depart under three or four weeks. A writer in the "Twentieth Century Practice of Medicine" estimates the duration as from four

to six weeks, according to the patient's surroundings and the atmospheric conditions. Asthmatic attacks may last from a few hours to three days and disappear suddenly. Morell Mackenzie states that attacks last from a few hours to several days, or even longer, finally ceasing almost as suddenly as they came, and leaving no trace either in local lesions or in systemic disturbance. Bosworth gives eighty cases, showing the durations of the annual attacks as follows:

From	May	1	to	frost	1 case.
“	“	15	“	May 25, to July 1	3 cases.
“	“	10	“	Aug. 1	1 case.
“	June	1	“	July 1	2 cases.
“	“	1	“	“ 14	1 case.
“	“	1	“	frost	5 cases.
“	“	10	“	July 4	4 “
“	“	10	“	“ 26	5 “
“	July	1	“	Sept. 1	1 case.
“	“	10	“	Aug. 1	1 “
“	“	10	“	Sept. 1	1 “
“	“	25	“	frost	4 cases.
“	Aug.	10	“	Aug. 27, to frost	51 “

All forms of hay-fever terminate with the first frost, and the long interval in which one may suffer is shown by the first case above from May 1st to cold weather. In the United States some who are attacked in May recover by the 1st of July; some attacked in July are well by the 15th of August; some attacked in August recover by November 1st, while some unfortunates suffer throughout the period from May to November. The June type may be followed by a September visitation or become a permanent August attack, or the August type may disappear in certain individuals and reappear as a June cold.

4. Symptoms

Altho the affection is called hay-fever, there is seldom any degree of pyrexia, and, as a fever, it is not a decided one. There are two well-known types of

the disease,—the catarrhal and the asthmatic. The onset of an attack is occasionally marked by feelings of general malaise, a loss of appetite, and depression of spirits. Indeed, these symptoms more or less characterize the entire course of the attack. A "tickling in the roof of the mouth" one week before the onset was felt by a patient of Sajous. Another speaks of dull pains in the head and back two weeks before; chills and shuddering ten days before the attack is experienced by another, while a large proportion complain of palpebral pruritis from two to ten days before the onset of the nasal symptoms. It is only in those subjects whose hay-fever is of some years' standing, Sajous points out, that the premonitory symptoms are present, and gives in evidence the testimony of a fellow-physician, viz.: "My attacks for some years

past came with much regularity, about August 12th to August 14th. On these dates this year I arranged to be on the water, on Lake Ontario and the St. Lawrence River, and entirely escaped everything like sneezing and irritation of the nose and eyes. Still I had the usual hot and slightly irritable skin, then an eruption of urticaria, accompanied by disordered stomach. This experience is precisely the same as in 1880, except that then I was on the Atlantic." Macdonald, in 1893, had a patient whose earliest symptoms were a curious coldness and pallor of the nose even in warm weather. In this connection it may be observed that in 1870 Roberts conceived the "pathognomonic symptom" to be coldness of the tip of the nose.

Beard divided the symptoms into local and constitutional. Among the latter he

regarded fever, loss of strength, the altered appetite and the nervous system, considering under this last, depression, indisposition to labor, sense of fulness and heaviness of the head, pain in the forehead and behind the ears, partial deafness, restlessness at night, inability to sleep, a sense of suffocation, and general irritability. For the local phenomena, he looked upon the skin, in the heart, chest, mouth and nose, eyes and ears.

The periodicity of the attacks is a prominent symptom and is difficult to explain. Some peculiar psychic influence occasionally acts to precipitate an exacerbation. In no other way can we explain the cases of John N. Mackenzie and Morell Mackenzie already cited. Analogous to this remarkable periodicity are those cases of intermittent fever wherein each alternate day, at a given hour, the chill occurs. This

is generally true, moreover, not only of ourselves, but of the world around us. As Holmes has beautifully shown in this connection, health and disease afford abundant illustration: The fixation of the number of heart-beats, of the respiratory movements, of the cycle of menstruation, or of the period of gestation are all recognizable in their unfailing occurrence, but their determination thereof, then, rather than at some other period, can not be explained. So, in disease, are the mutations of the enteric temperature, the recurrence of the hectic, of the regularity of the return of the type of ague upon the second, third, or fourth days, or of hay-fever upon its annual date. We must recognize these phenomena as fixt, further we can not go. "As the rhythm of physiologic effects is under the control of the central nerve ganglia, and as inter-

mittency is a peculiarly marked feature of so-called nervous disorders, so far the annual return and the variations are evidences of the neurotic origin of hay-fever."

The onset of an attack of hay-fever begins with a sense of irritation referred to the upper nasal chambers, a sense of fulness or tightness across the bridge of the nose. There is an itching or burning sensation of the inner canthus of one or both eyes, which may be accompanied by convulsive movements of the eyelid, an itching or tingling in the roof of the mouth. Spasmodic sneezing soon occurs, and pain in the eyeballs and in the frontal regions develops. The paroxysms are more or less violent and prolonged. Arnold tells of sneezing in a patient for twenty-five times in close succession, forcing the pulse at the height of the attack

to one hundred and twenty beats to the minute. These paroxysms are followed by an abundant, thin, serous discharge from the nose. The mucous membrane of the nasal fossæ swells so as to block up the nasal passages, and respiration through the nares becomes impossible. The escape of serum from the nostrils seems to increase the intense irritation and makes the sneezing worse. The discharge from both eyes and nose gradually grows thicker and may become semipurulent. There is often a certain amount of painful vision, and sometimes swelling, besides the usual pricking and stinging of the conjunctival surfaces. There are frequent transient paroxysms of lacrimation, and there is often much swelling of the eyelids as well as of the conjunctiva. The face becomes puffy and edematous, and the senses of taste and smell become im-

paired. The pharynx, mouth, and tonsils share in the engorgement and become red, and simultaneously the inflammation of the eyes, nose, and throat becomes intense and painful. Swallowing may become so difficult that there is little rest night or day. Insomnia is common and is often attended by nervousness and a sense of suffocation out of all proportion to the gravity of the condition. Cough is not a constant feature, but in a considerable proportion of cases it comes on in the second week, and lasts through the attack. Generally it is spasmodic and so incessant at night that sleep is impossible, and there are soreness and pain resulting from the straining of the diaphragm and intercostal muscles. Bronchitis does not usually result, and expectoration is absent or scanty until late. Cough may continue after all other symptoms have ceased.

The pulse and temperature are not generally altered, but later in the attack the temperature may be raised two or three degrees, doubtless from disturbed rest. A "sufferer" records that, in some, the genito-urinary and rectal passages give the first warning by intense itching and burning. In one instance, a more than generally severe paroxysm induced rupture of the capillaries in the lacrimal caruncle of the right eye, causing engorgement of the organ and displacement of the visual axis, with consequent double vision for some days. The direct and reflex changes in the vocal apparatus vary from loss of timber and harshness to complete inability to utter nasal vowels and consonants.

The disorder varies much in intensity even in the same person within short intervals of time, so as to almost give

an intermittent character to the complaint.

The attack finally ceases almost as suddenly as it came on, leaving no trace of local lesion or systemic disturbance. It is accompanied in some patients with nettle-rash. Asthma is a late symptom, coming on after the acute symptoms have abated, and cough has existed for some time. It may appear at the height of the attack. It is more common in autumnal catarrh than in the early forms. Its period, as a rule, begins at the fourth week, and it does not vary from ordinary asthma. It is sometimes periodic, occurring at the same hour night after night. Paroxysms appear associated with antecedent bronchial rather than nasal symptoms. Nasal reflex phenomena, without cough, may occasion paroxysms. Persistent cough more usually exists in the intervals between

paroxysms. Beard says that four-fifths of the sufferers have cough or asthma. The symptoms are not usually of equal severity each year. Asthma generally comes on in the daytime, a little ropy mucus being expectorated, and later an abundant frothy secretion. There may be only a slight remission, the dyspnea continuing so long as exposure continues. The attacks rarely produce emphysema of the lung, and sooner or later recovery ensues. Bosworth estimates that the asthmatic attacks come on earlier each year in those who have suffered from hay-fever in connection with asthma, and he believes that an attack of hay-fever is especially liable to develop an attack of bronchial asthma as a natural consequence of the disturbance in the nasal chambers. He also observed a number of cases in which hay-fever symptoms gradually abated while

the asthma became a prominent factor, and, again, that victims of hay-asthma finally acquired the perennial form of the disease,—the attacks occurring at all seasons without reference to the presence of pollen in the air.

As already evidenced in Sajous' case, in a number of cases the attacks are preceded by cutaneous eruptions. Laflaive cites cases with urticaria and eczema preceding the onset of hay-fever. Facial pruritis and herpetiform eruptions are occasionally seen. J. N. Mackenzie speaks of an inflammation of the external auditory meatus in all respects analogous to that of the nose in hay-fever, occurring repeatedly in a lady during the summer months.

Besides asthma, already mentioned, there is little tendency to permanent ill-effects except thickening of the nasal mu-

cous membrane from the prolonged irritation. Taste and smell may be impaired during and for a long time after the attack. General irritability and nervousness may be more or less persistent. Elderly sufferers for a long time may have weakened hearts which intermit during attacks, which may recover with returning health or result in cardiac dilatation. Wyman mentions pneumonia in three cases during attacks. In one case the catarrh ceased for two weeks to return after the pneumonia disappeared, when asthma also came on for the first time.

5. Its Pathology, Diagnosis and Prognosis

Morell Mackenzie states that hay-fever, leaving no permanent structural lesion behind it, can not, therefore, be strictly said to have any pathology. Surely it is that

no distinct specific organisms have been found. Sajous calls attention to the distinct physiologic functions of the two regions of the nasal cavities, the olfactory and the respiratory. The filaments of the olfactory nerve cover the superior turbinated bones, and the upper third of the middle turbinated bones, and the corresponding portion of the septum. Thus the upper portions of the nasal cavities are devoted to the sense of smell and do not enter into the pathology of hay-fever. The respiratory portion of the nose includes all the surfaces below the olfactory. It is under the control of the vasomotor nerves of the sympathetic system, and is quite sensitive to local or peripheral irritation. This sensitiveness resides in the terminal filaments of the sensory nerves, distributed over the surfaces of the mucous membranes. The mem-

branes of the posterior areas of the nasal fossæ are supplied with several branches of the sphenopalatine ganglion, which enter by the sphenopalatine foramen. This ganglion possesses a sympathetic root derived from the carotid plexus through the vidian nerve, thus establishing a connecting link between the nasal mucous membrane and the sympathetic system.

In health the nasal mucous membrane pours out from twelve to sixteen ounces of watery serum daily, which—that it may warm, moisten, and cleanse the inspired air on its passage to the lungs—is diffused over the convex surfaces of the turbinated bones. The centers in the medulla, through the vasomotor, control and regulate this process of serous exudation; the nicety of which regulation is seen in the adjustment thereof to the varying hygroscopic and thermic conditions of the air.

The experiments of John N. Mackenzie, in 1884, showed:

1. That in the nose there exists a well-defined sensitive area whose stimulation, through a local pathologic process or through an extra irritation, is capable of producing an excitation which finds its expression in a reflex act, or in a series of reflected phenomena.

2. That this sensitive area corresponds, in all probability, with that portion of the nasal mucous membrane covering the turbinated corpora cavernosa and the most sensitive spots covering the posterior end of the inferior turbinated body and the septum immediately opposite.

3. That nasal cough is caused only by stimulation of this area.

4. That the tendency to evolution of reflex phenomena varies in different individuals, and is probably dependent upon

the varying degree of excitability of the erectile tissue.

These sensitive areas correspond to the distribution of the sphenopalatine branches of the superior maxillary nerve, as distinguished from the nasal branch of the ophthalmic, which latter supplies the more anterior portions of the nasal fossæ. The former nerves, derived through the ganglion of Meckel, therefore, probably contain the vasomotor nerves which govern the erection of the turbinated tissue, and, hence, the localization of the sensitive areas becomes the key to the mechanism of the paroxysms. Nevertheless, Beard was inclined to transfer the point of greatest excitability from the peripheral ends of the nerve-filaments to the nerve-centers themselves, because it seems a more comprehensive explanation of the varied phases of the disease.

Roe explained that the more frequent occurrence of asthmatic paroxysms at night might be brought about by the gravitation of blood to, or the contact of polypi upon, these sensitive areas. Sajous thought it was evident that there were three areas capable of producing reflex symptoms in the course of a paroxysm of hay-fever, and that the three combined formed the key to the local nervous element, not that the three areas must take part, but in some, one of them, in others, two of them, etc. In the asthmatic cases, he noticed that both anterior and posterior areas were sensitive, the latter especially so.

Capp pointed out two distinct spots or areas of the mucous membrane of the nasal cavities, one at the posterior and one at the anterior extremity of the inferior turbinates, one or both of which

may be supersensitive in individual cases; also a spot in the anterior nasal chambers at the upper angle formed by the septum. All these are exquisitely sensitive, and, when irritated, produce extensive reflex symptoms. Trouble appears to begin at one or all of the points, while the rest of the Schneiderian membrane is in normal condition; but with sneezing, hyperemia and hyperesthesia ensue, and, through continuity, may extend to throat, ears, and eyes.

In speaking of the three reflex areas, Holmes said that it is regarded that all points of the cavernous tissue are not equally susceptible to irritation; the sensitive areas are the inferior turbinates (the posterior and middle reflex areas) and the portion of the septum immediately opposite, being particularly related to cough and asthma; the anterior, in the

vestibule, to sneezing, lacrimation, and other catarrhal symptoms. We might compare these reflexes with certain other cases of reflex asthma (not hay-fever) benefited by removal of the tonsils.

Bosworth regarded the continuous sneezing as pathognomonic and holds that the hyperemia is "confined entirely to the large venous sinuses, the capillaries proper not being congested," and speaks of the watery, serous discharge with the bluish-gray "tinge of the mucosa verging on opalescence, the surface of the membrane being covered with slightly viscid, watery serum, which gives it a glassy, semitranslucent aspect."

During an attack of hay-fever the erectile tissues of the nasal passages and the posterior throat become distended, the blood-vessels are engorged, groups of lymph-cells fill the lymphatic spaces, the

mucous surface is crowded with migrating leucocytes (white blood-corpuscles), younger epithelial cells are vacuolating and proliferating, secretion is increased in quantity and altered in character and composition, sensation is heightened, intensified, altered, or benumbed, and the whole metabolism of the affected region is profoundly disordered. Examination of the lower borders of the turbinated bones will disclose the mucous membranes of the nasal cavities arranged in thick, loose folds, owing to the peculiar distribution of the network of arteries and veins which go to make up "cavernous tissue." It is peculiar to this tissue that it may suddenly be engorged with blood, extremely distending it, and as suddenly emptied and the engorgement relieved. It is especially thick over the inferior turbinated bones and over the lower and posterior part of

the nasal septum, and also upon the lower edge of the middle turbinated bone. In acute conditions the engorgement and distention soon subside. In chronic states the mucous membrane becomes markedly thickened and the blood-vessels enlarged and tortuous. The subsidence of the engorgement can not occur, and as a result there is a greater or less degree of closure of the nasal passages.

The mucous membrane of the nasal cavities in hay-fever does not present the characteristic features of an acute inflammation. The impact of pollen or exciting irritant causes complete relaxation of the large veins of the turbinated bodies and an exudation of serum, which relaxation continues so long as pollen or the irritant is *in situ*, but as soon as it is removed the normal caliber is again restored and the attack subsides. Deviations of the sep-

tum or chronic rhinitis are occasionally found concurrent with the disease, but can not be regarded as characteristic.

Hay-fever may be distinguished from asthma, common catarrh, bronchitis, acute rhinitis, remittent fever, and catarrhal conjunctivitis. The salient feature of hay-fever is its periodicity or annual recurrence. This is part of its very nature, is the central point of diagnosis, is its chief characteristic, and to its elucidation, Holmes says, all existing theories tend.

Beard states that hay-fever is like asthma in the following points:

1. It is hereditary;

2. It is more or less periodic;

3. It is paroxysmal;

4. It is correlated to other functional nervous affections;

5. The paroxysms are excited by a great

variety of irritants; persons being differently affected;

6. It is singularly obstinate and is relieved by the same remedies.

Bosworth considers hay-fever dependent upon:

1. A neurotic habit;

2. Pollen in the atmosphere;

3. A disordered condition of the nasal passages.

While asthma is dependent upon:

1. A general neurotic condition;

2. Obscure conditions of the atmosphere;

3. Diseased bronchial (not nasal) mucous membranes.

It is the comparative suddenness of the onset, as well as its sudden departure, the violent paroxysms of sneezing, and the character of the nasal discharges which are the peculiar features of hay-fever.

The first attacks are likely to be mistaken for ordinary coryza, but here the abrupt onset, the characteristic edematous puffiness of the eyelids, the absence of constitutional symptoms will indicate the difference. In children, moreover, attacks of hay-fever are most liable to be mistaken for acute colds or rhinitis,—but here, again, the above points may serve to distinguish, together with the sequence of the symptoms, the time of year, and the physical signs of an acute bronchitis, if it extends so far. The approach of cold weather and the coincident departure of the symptoms will make clear a diagnosis, while the history of previous attacks at the season of the year most favorable to hay-fever, the presence of certain irritants, and the general condition of the bodily symptoms may be of aid in distinguishing the affection. In acute rhi-

nitis there are several stages, viz.: First, a dry stage, lasting for a few, say twelve, hours; second, a serous discharge lasting two or three days; and, third, a muco-purulent discharge for from three to five days,—while the entire attack runs its course in from five to ten days if no complications ensue. In hay-fever there is no dry stage; the discharge from the outset is purely serous and never muco-purulent during the entire course. The nasal discharge in hay-fever is sometimes slightly opaque, and it may contain some few epithelial cells and viscid mucus. In acute rhinitis examination of the nares will show an inflammatory area while hay-fever shows none. Hay-fever is a vaso-motor paresis, and is easily diagnosed from inflammatory coryza by the swollen bluish-gray appearance of the inferior turbinated bones, and by the fact that the

first train of symptoms continues through to the end. Examination of the nares will disclose occlusion due to the swollen turbinated bones lying in contact with the septum. The appearance of the mucous membrane itself is characteristic and only slightly resembles an inflammatory process. It is markedly swollen, not bright red as in rhinitis, but bluish-gray, covered with a thin, slightly viscid, watery serum, giving it a glassy, semitranslucent, at times opalescent appearance. Again, the marked puffiness of the eyelids, the great suffusion of the eyes, the photophobia, and even epiphora are distinguishing features of hay-fever.

The sensitive areas spoken of, particularly those on the lower and posterior parts of the septum and the inferior turbinated bones, are of value in differentiating hay-fever, and the markedly pro-

nounced paroxysms of sneezing are very prominent in hay-fever.

People are subject in the changeable climate of spring and early summer to catch colds, and especially is this true of those prone to catarrh. These cases are sometimes mistaken for hay-fever. The readiness, however, with which they yield to anti-catarrhal treatment shows their nature.

The prognosis is invariably good as to life. Sufferers often live to advanced ages. Hay-fever is no bar to life-insurance, but unless rationally treated the chances of permanent cure are very small. There are few exceptions to the rule that the tendency is, when once established, to an annual recurrence, unless the predisposing causes are removed, or there is removal of or away from the exciting cause. Beard states that hay-fever has

no effect on longevity, and that, judging from observation and analogy, this affliction may act as a kind of safety-valve for the nervous diathesis, preventing other and more serious disorders, and thus becoming the friend rather than the enemy of life. When once attacked, unless properly treated, escape is rare in any subsequent year. Even changes in constitution in extreme age are no bar or protection. It rarely skips a year, provided locality and influence are the same. Absolute immunity is only obtainable at the price of temporary exile. There is no proof that hay-fever is generally milder or severer in certain years all over the world or over a country, yet evidence is satisfactory that in certain localities it varies greatly in different years.

Now and then, but not often, the tendency to the disease seems to be out-

grown. In one of Beard's cases the disease skipped two years. Dr. Gibbons, of California, mentions a terrible case in which the attacks in successive years became lighter and lighter and finally disappeared entirely.

With respect to increase or decrease of severity of symptoms with advancing years there is no constant law. In some cases the disease grows milder, in others severer, in others still, years of comparative mildness alternate with years of comparative severity. The early form may change into the later form. There is no doubt, however, that attacks may change from the early to the late form, and *vice versa,* and in advancing years may be milder. Bosworth states that the younger the patient the better is the promise of relief; and that rose-cold, belonging more especially to early life, is to be regarded

more favorably than other forms. Macdonald has observed spontaneous disappearance in children, perhaps due to an increase, *pari passu* with growth and development of nervous stability.

As regards the termination of each individual attack the prognosis is invariably favorable; *cessante causa, cessat effectus.* There is almost equal certainty that with the same causative influences the attacks will reappear upon exposure to the exciting cause. It is peculiar, too, that the disease of one year's standing has proved as obstinate as one of from twenty to thirty years' duration. In these instances it may be a question as to how firmly fixt has become the neurotic habit.

W. W. Bulette, of Colorado, in 1896, as a result of his own experience, made the assertion that more than eighty per cent.

of hay-fever sufferers can be permanently and effectually cured. Thoro examination of the patient and elimination of every possible source of irritation and pathologic condition are necessary.

I desire to be more emphatic, and from my results in the treatment of over 200 cases during the last twenty years, I believe that the curability of the disease can not be questioned. That all cases can be cured is questionable; but we can unhesitatingly say *that a majority of cases are curable, and that positive relief, without change of residence or inconvenience, can be afforded during the period of occurrence, if treatment is directed along the lines laid down in the following chapter.*

PART II

ACCEPTED CAUSES

PART II

ACCEPTED CAUSES

1. When Due to Some Exciting Agent Such as Pollen

It being generally recognized that there are two elements entering into the causation of hay-fever, viz., an exciting agent and a predisposing or preexisting condition, regard will be given the subject of causation from this standpoint.

A great number of agencies have been regarded as the direct causes of this disease, but opinion in the main has assigned pollen as the essential factor, acting upon the preexisting condition or predisposition. It may be better, however, to give a résumé of other agencies before

regarding this subject of pollen. The most important of these are heat, light, dust, ozone, overexertion, ipecac, lycopodium, coumarin, benzoic acid, chocolate, or several of these in combination.

No attempt to signify or designate a definite cause was made by the early writers until 1819, when Bostock first described the malady and ventured the view that it was due to the influence of solar heat. He attributed his own prolonged sufferings to the exposure to the sun's rays and fatigue.

Some time after, Phœbus attributed the affection to "the first heat of summer," which, he stated, "is a stronger cause than all the grass emanations put together." Phœbus subsequently modified his views so as to regard the first heat of summer as acting only in an indirect manner as an exciting cause, and admitted

that hay and the blossoms of rye caused exacerbations. It can not be contended, at this day, that heat alone will provoke the disease. In the plains of India when the heat is greatest it is not found, altho later in the year, in the cooler months and before vegetation is burned up, it does appear; but among the hills of India, where the climate is milder and the grasses and cereals are in blossom, hay-fever exists. At sea, when vessels are becalmed and heat is most intense, and in the great heat of the desert hay-fever is not found. Pirrie shows that great heat is common to all cases, even when the vegetable world is looked to for the cause, and strangely points out that the premonitory feelings of an attack coincide with those caused by high temperature. One of the most interesting cases from this standpoint is that of an En-

glishman, who, altho not a medical man, was well known to science—Richard Proctor. The asthma—for it took this form — occurred only during the cold months, and was always aggravated by a rime or hoar-frost, especially if the latter was followed by a bright, sunny day.

It is a striking fact that in regions comparatively free from the disease persons subject to it become worse on warm days, or when the wind blows from the south. It has been found by experience that while this aggravation by winds is in most part due to the presence of more pollen, the higher temperature is also in a measure responsible. Hot, dry days are more favorable to the dissemination of pollen than rainy ones, and it becomes especially active when hot, dry periods follow stormy weather. In the light of Blackley's experiments upon the amount

of pollen in the atmosphere, these facts would seem to explain the action of heat and sunlight as an active cause in the production of the exacerbations of hay-fever.

Phœbus was dissatisfied with the view of the influence of solar heat, and thought that the longer days, which produce a more continuous action of light, were perhaps to blame; but where light is strongest and lasts the longest—indeed, in the land of the "midnight sun"—hay-fever is practically unknown. Pirrie called attention to the fact that exposure to strong light aggravated the symptoms of the attack. The cited case of the late Richard Proctor is an example of the truth of this. There is an instance of the widow of a clergyman whose attacks, most severe in summer, were aroused by sunlight in the early morning. Ingals knew a clergyman who was unable to cross the street

on a hot day without sneezing violently unless he carried an umbrella. Persons with sensitive mucous membranes, especially subjects of hay-fever, are, no doubt, sometimes liable to attacks of sneezing from sunlight; but these symptoms must not be mistaken for true hay-fever. Ingals states that he knew an individual in whom attacks of sneezing were brought on by exposure to bright gaslight. Gaslight was also regarded by Beard as a cause of this affection. However, Morell Mackenzie shows that gaslight is employed more in winter when the affection does not prevail than in the English spring and American autumn, when the affection most prevails. Nothing can exceed the reflected glare of sunlight at sea on a bright day, yet it is upon the sea that exemption from attacks of hay-fever is universally found.

From his scientific investigations upon the subject, Beard, whose published work is a model, concluded that it was extremely probable that dust occasionally caused hay-fever. Out of 198 cases of hay-fever reported by him no less than 104 attributed the affection to dust. One hundred and forty-two of these cases, however, occurred between May and September, the usual hay-fever season; and the lay, not the trained professional, mind advanced the causes. Some attributed the affection to "indoor dust"; some to "cinders." These data of Beard, therefore, must be taken *cum grano salis*. More especially is this so since a paroxysm of sneezing and subsequent coryza, frequently brought on in normal health by the mechanical irritation of dust or even strong odors, should hardly be dignified as an attack of hay-fever. In England,

in February, March, and April, when strong east winds often blow clouds of dust against the face, the symptoms of hay-fever do not appear, whereas in June and July, when dust is comparatively little, the affliction is most extant.

Holmes stated that even in winter-time stirring among old books or in an old garret the exposure to the fine dust therefrom would, by simple mechanical irritation, produce an attack in him. It has been the consideration that dust, or pollen, acting as any other form of dust, could be kept from entering the nasal chambers that has given rise to the various inventions to purify the air before it enters the nose, such as plugs of cotton or wool, and veils (which, in addition, soften the glare of the sun and lessen the irritating action of winds. Every hay-fever sufferer knows the little value of such a device.

From the vast quantity of facts and observations gathered together by him, Phœbus, who previously had ascribed sunlight as the cause of hay-fever, endeavored to extract a complete theory of the disease. He suggested an excess of ozone in the atmosphere as a possible cause. It remained, however, for Blackley, in 1873, by his great endeavors and scientific methods of investigation, to disclose the fallacy of this theory. He purposely breathed air highly charged with ozone for five or six hours without effect; and without inconvenience he inhaled ozone artificially prepared and in quantities far exceeding that found in the same volume of atmospheric air. This same physician also studied upon himself the effects of benzoic acid, a substance shown by Vogel to be contained in *Anthoxanthum odoratum* and *Holcus odoratus,* the

two species of flowering grasses to which the causation of hay-fever has been attributed. Likewise he investigated the odorous principle of many flowering grasses, coumarin, and the volatile oils which impart to many plants, such as peppermint, juniper, rosemary, and lavender, their characteristic perfume. In all these cases the results were negative.

Various other exciting causes are in numberless variety and many of purely idiosyncratic nature. Emanations from dry hay, sunlight, gaslight, heat, minute organisms as supposed by Helmholtz, the "mange" insect, dusts of all kinds, bad air, railway smoke, brimstone matches, flowers and fruits, odors from dogs, cats, horses, cattle, rabbits, guinea-pigs, and wild animals, have all been held responsible for the paroxysms. Ward Smith records linseed meal and mustard as

exciting causes. Wm. Murrell mentions powdered May-apple (podophyllum), the effluvia of clean pocket handkerchiefs fresh from an ironing table, locust-tree blossoms, mulberry blossoms, and fruit. The exhalations from feathers have been regarded as causes. It is well-known that various drugs like ipecacuanha and lycopodium give rise to attacks, and sulfur has been mentioned as a cause. Sir Thomas Watson names a servant in St. Bartholomew's Hospital affected by ipecac. Cullen tells of an apothecary's wife who, whenever ipecac was triturated in the shop, had an attack of hay-fever. He also mentions the vicinity of a rice-threshing floor as a provocative cause. Itzigson tells of a merchant who had hay-fever paroxysms whenever fresh coffee was handled in his presence; and it is recorded of a dyer that he could not work

when the wood of the oak (*Quercus tinctoria*) was lying about. The author knows of a case in a physician in whom violent paroxysms of sneezing are induced by the tasting of chocolate. It is related in the "Twentieth Century Practise of Medicine" that a hay-fever patient fond of tomatoes and watermelons was unable to eat of them during the usual hay-fever season without most violent disturbance of the gastro-intestinal tract. Bastian was subject to attacks of an affection like hay-fever while dissecting the Ascaris megalocephala, a parasite infecting the horse. Hyde Salter tells of a clergyman affected by the vicinity to a dead hare, and who was thus able to detect the presence of a poacher. H. Charlton Bastian had like effects from the "mange" insect of the horse. Ringer and Murrell tell of a young gentleman

made worse by the vicinity of horses or stable people. Once, while in the theater, an attack suddenly supervened without any appreciable reason until a horse galloped upon the stage. Macdonald, in 1893, mentioned a patient who, two or three hours after having patted his horse with his gloved hand, inadvertently put it to his face, and was immediately seized with a violent paroxysm. The odor from the inner aspects of the legs of the horse was very irritating to one writer, a "sufferer." Ringer and Murrell cite the case of a gentleman who, subsequent to an acute pleurisy, was ever after a subject of "hair-caterpillar asthma," and was immediately attacked if by any chance he touched a caterpillar.

The difficulty of sometimes finding some exciting agent is shown by the case of Drenger. After searching several

years in vain for the cause of attacks of hay-fever caused by entry into a certain room in a house, and after ransacking nearly everything in the house, a mattress was suspected, and, upon removal, was satisfactorily shown to be the offending agent.

The odor of peaches, of violets, of the mignonette, of chocolate, of musk, and of peppermint, has come in for a share of the blame. Trosseau relates of himself that attacks came on when he entered a room in which there were violets. The botanist Broussais was often impeded in his work by attacks caused apparently by the odor of a rose. Hünerswolff and Morell Mackenzie each cite a case in which the perfume of the rose produced attacks of coryza. The former's account is in the "Ephemerides," and has been often referred to. The latter's case proved rebel-

lious to treatment, and the sufferer had, at last, to banish these flowers from her garden. That this peculiar antipathy to flowers is often imaginative is also shown by John N. Mackenzie, who cites the case of a subject of hay-fever to whom he handed an artificial rose. Immediately an attack of rose-cold ensued. A patient mentioned by Phœbus and Morell Mackenzie, while gazing upon a picture of a hay field, was seized with an attack of hay-fever. These last two instances indicate the psychic influence rather than any extraneous cause, but they serve to show the varieties of exciting agents.

The external cause which has been by far the most generally recognized and accepted as the most frequent is pollen. The older writers upon this theory did not distinguish the underlying condition necessary before pollen could act as a cause of

the disease. The remarkable and elaborate experiments of Blackley, from 1866 to 1878, conclusively prove that a most important exciting cause of hay-fever is found in the action of pollen upon the mucous membrane of the nasal cavities. In his own person he showed that the inhalation of pollen always brought on the symptoms of hay-fever; that there was a direct relation between the intensity of the symptoms and the amount of pollen in the air, and that none of the other agents referred to, such as heat, light, ozone, dust, or odors, would, of themselves, cause the distress. His range of observation included the pollens of various grasses and of cereals and of plants of thirty-five other natural orders. His experiments were made in the hay-fever season in England, between the end of May and the latter part of July, and showed

that ninety-five per cent. of the pollen contained in the atmosphere belonged to the *Graminaceæ.* The apparatus from which he obtained the most satisfactory results in his investigations consisted of a vertical plate of glass, $7/8$ of an inch in diameter. It was covered with a hood, and was pivoted to an upright staff. A weather-vane surmounted the hood to control the face of the glass-plate before the wind. Upon this glass-plate was affixt a microscopic cover-glass, one centimeter in diameter, covered with glycerin. Any pollen floating in the atmosphere would thus be carried upon the plate by the wind-current and adhere to the glycerin upon the glass-slide. Blackley thus found that the amount of pollen caught upon the plate increased progressively from the seventh to the thirtieth of May, when twenty-five grains were counted, to seventy-six grains on the

eighth of June, and to 280 grains on the tenth of June. On the twenty-eighth of June 880 grains were counted, after which date they decreased until the first of August, when they had completely disappeared. Bright, sunny days brought large quantities of pollen, while rainy days decreased the amount. Passing showers ameliorated the individual symptoms, tho not affecting the amount of pollen deposited upon the slide. Blackley also clearly showed that the mucous membranes of the nasal fossæ were not affected by pollen in the atmosphere when twenty-five grains per diem only were deposited on his glass, while seventy-five grains in twenty-four hours would irritate in certain individuals. When 280 grains of pollen per day were deposited the direct action upon the mucous membrane of this quantity would result in complete vascular dilation.

Clinical observation has shown a parallel, but by no means a complete, analogy to the above phenomena in the action of cocain in different strengths of solution.

Emanations from the rose and from rye have been shown to have caused coryza, occlusion of the nostrils, and sneezing for from six to eight hours. The sweet-scented vernal grass (*Anthoxanthum odoratum*), sweet-scented soft grass (*Holcus odoratus*), meadow grass, meadow fox-tail, Indian corn, barley, wheat, oats, bean-flowers, lilies, elder trees in bloom, the goldenrod, hay, timothy, and clover, and others may be mentioned. In America the pollen of the Roman wormwood, ragweed, or hogweed (*Ambrosia artemisiæfolia*), is the most commonly referred to. It is very common in nearly all the States. It blossoms in August and September, the prevalent time of hay-fever. Wyman and

his son, who had fled to the White Mountains to avoid hay-fever, were immediately attacked when a package of the ragweed was opened there. The seashore, usually exempt, sometimes is not so, probably due to the presence there of the pollen of the *Artemisia gallica,* another kind of wormwood. In England the *Anthoxanthum odoratum,* or "sweet-scented vernal grass," seems especially causative. There must also be mentioned the common daisy (*Bellis perennis*) of England; also the rye-grass (*Lolium perenne*) and "sweet-scented soft grass" (*Holcus odoratus*). In Germany the rye-blossom is chiefly indicated as a cause. In Australia the Cape weed pollen is regarded as most commonly provocative. It covers the hills round about Adelaide to the height of some thousand feet or so. Most of the population of Adelaide is affected with

hay-fever during the time of its blossoming, viz., in September. In India, where the malady occurs chiefly in February, it is the blossoms of the mango-tree (*Mangifera indica*) that are held responsible.

J. C. Wilson holds that most subjects are not sensitive to emanations from hay, and points out that there are no distinctive bacteria to give rise to the affection. Marsh, himself a sufferer, stated his belief in the pollen theory, conceiving hay-fever analogous to *Rhus toxicodendron,* or ivy-poisoning of the skin.

There are two authentic cases which would impair the pollen theory, the well-known exemption of hay-fever subjects at sea being granted. One is mentioned by Walshe, in which a passenger retained his symptoms of hay-fever during a passage across the Atlantic. Abbotts Smith has reported the other, in which the disease came

on at sea nine miles from land. In this latter case, unfurling the sails in which a large quantity of pollen had been folded may explain the occurrence. In the former instance the diagnosis was by no means certain and the presence of some other irritant may have accounted for the distress. Moreover, it is by no means impossible for pollen to be deposited on a ship even when miles away from land. In speaking of the distribution of pollen Darwin tells of how the ground near St. Louis, in Missouri, has been so widely covered with pollen that it looked as if it had been sprinkled with sulfur. Pine forests, 400 miles south, were probably the place and distance from which it came. On March 16, 1883, in Philadelphia, ignorant people took for brimstone a shower of yellow pollen which had been blown from some distant pine forest.

After citing many of the various causative pollens Holmes says that he is "not aware that any specialized action has been proved; all act (if at all) by mechanical irritation." He also shows the punctuality of flowering on the selfsame date yearly is an absurdity, depending, as the flowers do, upon the variations of the seasons.

The date of the flowering of plants varies within certain limits, and he points out the mutability of the blossoming date, or, more rationally, its limited variation, and further adds that "even as a mere irritant, as pollen affects comparatively few, it must act upon a condition which is preexistent, which is, therefore, independent of and predominates it, else would the cause, pollen, produce it universally."

As already mentioned, it has been claimed, that a toxin generated from pol-

len by a fermentative process in an alkaline solution is the cause of hay-fever.

2. The Predisposing Causes

While millions of people are exposed to the exciting causes of hay-fever, comparatively few suffer from it, and that there is an underlying condition, predisposition, or idiosyncrasy, can hardly be doubted. Exactly what this is, or on what it depends, is unknown. Abbotts Smith, as early as 1865, spoke of a predisposition to attacks of hay-fever as one of the principal causes thereof. As Holmes has shown, there must be individual predisposition, since the exciting causes, if pollens, are everywhere. This predisposition or idiosyncrasy has generally suddenly developed without apparent reason. It has been argued that it is systematic or central, and that it is due to some local abnormality of the mucous

membrane, the capillaries, or the periphery of nerves. Once acquired, however, it is seldom lost, and it apparently increases with each successive year.

The influence of race is seen in the fact that the English-speaking people are the principal sufferers. In India, Africa, and Australia it is mostly the English and Americans who are attacked. In America it occurs in nearly every State, altho much more infrequently in the South. In Canada hay-fever is rare, especially in the maritime provinces. Wyman relates a case—the only one reported—of hay-fever in an Indian child. Beard mentions that Dr. Jacobi, of New York, who practised much among the Germans, had never met with a case in that nationality; and in the same city a similar observation was recorded by Dr. Chaveau, a practitioner among the French. Sajous has called at-

tention to a curious fact in this connection—viz., that the principal sufferers, American and English, are excessive tea-drinking nations, and that this beverage may exert a depressing influence on nerve-centers. It would be interesting to have some information as to the existence of hay-fever in China and Japan, the tea-producing countries. John N. Mackenzie, in 1884, gives the first recorded instance of hay-fever in a negro, a male of thirty-five, tall, well-proportioned, and respectable, the attack lasting from the second week in August to late in September. A sensitive spot was found on the left inferior turbinated bone, 1¼ inches within the nostril, which gave origin to a most intense paroxysm of asthma on simple contact with the probe.

Reports of hay-fever have come from nearly every quarter of the civilized globe.

It is seldom seen in the far North, and is more frequent in the temperate than in the torrid zone. It is seen more often in urban than in rural districts. The disease is by far the most frequent in Great Britain and the United States. In Norway, Sweden, and Denmark it is seldom found, and it is scarcely ever seen among the natives of Russia, Germany, France, Italy, or Spain. The English and Americans in India and Africa are the only ones who are affected by it. Macdonald, in 1893, said the Irish are certainly not exempt. In the north of Scotland it is very infrequent, while in the south of England the disease is more frequently found than in the north. In Australia and New Zealand it is occasionally found. Literature is strangely silent about South America, but this land is strange to us in many other ways. Pirrie gives an instance of an English officer in India suf-

fering there when vegetation was altogether different from the forms met with in England where his attacks had begun. As already noted, the complaint has made its appearance in two instances when its victims were at sea; one, reported by Abbotts Smith, after shaking out the sails when nine miles out at sea; and another, reported by Walshe, in which the patient suffered throughout a voyage across the Atlantic. A "sufferer" records that numerous portions of England, especially the highlands and the seacoast, and nearly all of Wales and Scotland are exempt from the disease. He also regards the upper side of the St. Lawrence River, most of the province of Ontario north of the Welland Canal to the Detroit River similarly exempt, and he states that the disease is wholly unknown to regions above the outlet to Lake Huron.

Wyman has considered the regions of America where hay-fever is especially prevalent. That portion of country east of the Mississippi River and lying between the 35th and 45th parallels of latitude he regarded as the territory of prevalence. Canada and the Adirondack Mountains, the Appalachian range, and the elevated plateau throughout New York State he considered almost exempt from hay-fever. That portion of the United States west of the Mississippi River he seemed to think, as did Beard also in his later investigations, was free from the disease. Beard based his reasons upon the lack of vegetation and the sparseness of the population. Bosworth regards as better reasons the rugged mode of life of the inhabitants and the consequent vigorous health of the frontier life. It is a curious observation, too, that certain portions of the White Moun-

tains country, formerly regarded as invariably free from hay-fever, of late years, probably owing to the extension of civilization and its vegetation to these regions, are no longer exempt from it. Southern climates, to a certain extent, are exempt from the disease. Wyman thought it did not prevail south of the 35th parallel of latitude, with the exception of certain districts in the neighborhood of Milledgeville, Georgia, Montgomery, Alabama, and Beaufort, North Carolina. There can be little doubt that the affection is less common in Maryland, Virginia, in the border States, and in the far West; that it is rare in the extreme South and on the Pacific slope. The zone between the 35th and 45th parallels of latitude practically includes the hay-fever district. Even in this section, localities, from their proximities to large bodies of water or to oceans, to

elevation or to absence of certain vegetation, afford immunity. A "sufferer" states that on Lake Michigan hay-fever is absent above Ludington, while on the Mississippi, in Wisconsin, it is present as far north as the Chippewa River, and in some seasons, in a mild form, it is seen in St. Paul, Minnesota. It is known to extend to the latitude of Memphis in the West, Knoxville centrally, and Cape Henry on the Atlantic. In 1896 W. W. Bulette stated that in certain sections of Colorado there is a variety of the affection known among laymen as blossom or cotton-wood fever, and very prevalent in regions where the cotton-wood tree abounds. The symptoms are practically identical with those of the autumnal variety of hay-fever, except that the throat and bronchial irritations are intensified, and the course of the attack is somewhat shorter. Symptoms occur about

the 12th of April and terminate in the latter part of May, and rarely last longer than July 1st.

Beard's pamphlet was the first to show a radical departure from the pollen theory and to establish that the neurotic habit was an essential factor. He showed that subjects of hay-fever often acquired the affection or the tendency to it through inheritance. The facts sustaining this view are of "a most overwhelming character." Wyman, himself a sufferer, records numerous cases in his own family through four generations. He proved the powerful influence of heredity in many of his cases. It even appears in childhood, he states, and quite generally in those of nervous diathesis. In Dr. Morell's family there were six sufferers from hay-fever besides himself. In the family of Henry Ward Beecher there were two besides himself;

and Chief Justice Shaw's family contained seven. Bosworth says that eighteen of eighty cases disclosed direct heredity, while in thirty-nine there was either hay-fever or asthma in the family. Of the forty cases of Sajous', thirty-five per cent. had near relatives who presented clear histories of hay-fever, and forty-two per cent. had asthmatic relatives, while fifty-three per cent. of these cases presented a family history of either hay-fever or asthma. Morell Mackenzie has several times treated father and children for hay-fever at the same time. Prince relates that five members of the same family were hay-fever subjects. One daughter of thirty years suffered with June cold ever since she was five years of age, every year save 1887, 1888, and 1889. Her grandmother, mother, and two brothers suffered alike. The daughter, convinced that mental or

nervous influence affected her, in 1887 was treated by the "mind cure," and for three years subsequently was free from her symptoms. When the original mind curist was dead, in the fourth year, the symptoms returned as badly as ever. Christian Science influence was tried in vain.

There can be little doubt that males are more afflicted than females. Of the early forms of the disease, however, females seem more susceptible than males. Of 433 cases cited by Phœbus, Wyman, and Beard, only 142, about one-third, were females. Of 506 cases gathered from several authors, 342 were males, 164 females. Morell Mackenzie met with 38 cases in males and 23 in females. Men are the more exposed to the exciting causes such as dust, heat, pollen, etc., altho females are the more neurotic. The proportion is about one female to three males.

Only to some extent can age be said to affect the disorder. The liability to hay-fever in the great majority of cases appears before the age of forty. The malady has been reported, however, as occurring for the first time in persons as old as sixty, and persons of seventy and upward have suffered. Of the cases of children who have been attacked the disease had manifested itself in the parents. It would have probably been regarded as a common cold, had not the parents been the subjects of the affection.

Most all writers on this subject have observed that the disease attacks the better educated classes and those of fair social position. It is rarely met with among the laboring classes. This would seem to emphasize the view that the disease is essentially a neurosis. From the notes of sixty-one cases of hay-fever in private practise,

and the sight of many others of which no record was kept, Morell Mackenzie found all the patients persons of some education, and recalled having seen none among his hospital patients. Of forty-eight cases of Blackley, all were educated, and Wyman made the same observation. Holmes has shown that the ignorant classes are not so likely to recognize the disease as a distinct affection, and apply for medical aid

The fact that the rustic is much less subject to this disease than the dweller in the city and town, shows the influence of the mode of life. Farmers and agriculturists, exposed, it would seem, far more to the exciting causes than others, are peculiarly less liable to suffer from it. Beard reports only seven such cases among 200. Morell Mackenzie states that it is impossible to tell whether the villager owes his exemption to the maintenance of vigorous health

by an outdoor life, or to habitual exposure to the cause of the complaint.

Holmes admirably points out that "a part of the mysterious origin must be set down to the indifference of the sufferers who, from year to year, have forgotten their periodical affection and failed to consult physicians." He says: "Of similar cause is the groundwork of the assertion that it affects only the wealthy. This is simply because with this class there is a higher intelligence and closer attention to ailments, and the fact that having once discerned the actual condition, they, in many instances, take professional advice or go to a place of refuge, thus drawing notice to themselves, all of which things are denied to the lower (poorer) classes. It is said that there are some 200,000 sufferers in the United States, at least within the range of observation of the Hay-Fever Association,

which, meeting annually at Bethlehem, N. H., may be held to represent the more stable and well-to-do. From my own experience and observation I am convinced that there are many of our working people who suffer from this affection who do not even recognize the disease." Merchants, professional men, persons of sedentary habits and brain-workers supply most of the victims. The disease is not so uncommon among hospital outpatients here and in England as formerly.

Concerning the influence of the neurotic tendency, Beard pointed out, in 1876, two popular misconceptions of the nervous theory, first, that nervous susceptibility implies debility and emaciation, whereas the nervous temperament is consistent with great strength and power of endurance, especially when combined with the bilious and sanguine temperaments; and,

second, that the nervous theory dispenses entirely with the influence of exciting causes, as heat, pollen, etc. Beard concluded that the disease is a complex resultant of a nervous system especially sensitive in this direction and acted upon by the enervating influence of heat and by any one or several of a large number of vegetable and other irritants, and this view has the advantage over other theories in that it accounts for all the phenomena exhibited by the disease in this or in any other country. He believed that the transmissibility of the disease from parents to children; the temperaments of the subjects; the capricious interchange of the early, the middle, and the later forms; the periodicity and persistence of the attacks and their paroxysmal character; the points of resemblance between the symptoms and those of ordinary asthma; the strange

idiosyncrasies of different individuals in relation to the different irritants; the fact that it is a modern disease peculiar to civilization; the fact that it most abounds where functional nervous disorders are most frequent and is apparently on the increase *pari passu* with other nervous diseases; and, finally, the fact that it is best relieved by those remedies which act on the nervous system,—all these otherwise opposing and inconsistent phenomena are by this hypothesis fully harmonized. Prince remarks that altho a nervous origgin has been recognized by some, still no theory has been proposed to show the connection between the physical symptoms and the nervous processes nor the pathology of the nervous processes themselves.

Vasomotor susceptibility has been viewed as indicating the neurotic tendency, and this may or may not be due to a central

lesion. John N. Mackenzie regarded disordered functional activity of the nerve-centers as the expression of the nervous origin. Again, a general neurosis disposing to vasomotor disturbance of the sympathetic and the trigeminus nerves has been held responsible. Kinnear speaks of two forms,—one a hyperemia, and the other an anemia of the sympathetic ganglion. Bosworth is inclined to think a peculiar lack of vasomotor control characterizes the neurotic manifestations. In asthma there is undoubted vasomotor paresis of the blood-vessels of the bronchial mucous membranes, while in hay-fever it is of the nasal mucous membranes.

Solis-Cohen regards hay-fever as generally a neurosis, primarily a vasomotor ataxia or idiosyncrasy. Another view is that it may be due to an organic alteration of the nerve-fibers terminating in the nasal

region and chiefly in three reflex areas. Again, that it may be due to functional activity or paresis of the governing (vasomotor) centers, accompanied by hyperexcitability of the erectile (cavernous) tissues aroused by peripheral irritation. The phenomena of the cavernous nasal tissue, tho secondary to the centric condition, indicates a vasomotor disease. Hack and Robinson believe the morbid lesion is one of neurotic disposition with hyperesthetic condition of the olfactory and fifth pair of cranial nerves.

Analogous to the neurotic habit is idiosyncrasy. Apparently the same understanding as to what an idiosyncrasy is has underlain the use of this word by various writers who have advanced idiosyncrasy as a cause of hay-fever. Morell Mackenzie, in 1880, put it down as a predisposing cause, but does not say upon what the idiosyn-

crasy depends, whether upon some local abnormality, the capillaries, the nerve-centers, or the periphery of the nerves.

In 1897 S. Solis-Cohen said idiosyncrasy is a real condition in hay-fever, and cited the idiosyncrasies to salicylic acid, quinin, ipecac, opium, etc., as similar to idiosyncrasies that patients exhibit toward the different irritants capable of producing hay-fever. Using the word to express the fact that certain persons react differently from most of mankind to certain forms of irritation, it means something. It means that such persons are abnormal, altho the cause of the abnormality remains to be discerned. Holmes, speaking of idiosyncrasy, would not say there is no such thing as idiosyncrasy, but as far as hay-fever went, he held that the disease was an actual one, the nature of which was not yet comprehended. He remarks that it is quite

probable that uric acid would aggravate hay-fever as it would any other condition in the body; and that some think to have proved this by the use of salicylic acid, to which drug many persons have an idiosyncrasy, thereby aggravating the condition in hay-fever by the elimination of uric acid.

Dr. Samuel Ashhurst, in 1897, recorded his habit of regarding hay-fever of late years as a personal idiosyncrasy acted upon by some irritant, and observed that without this personal element it is difficult to account altogether for the symptoms and their peculiar periodicity.

In 1882, Daly advanced the theory of the local disease as causative of hay-fever, and reported a case in which the patient recovered after the removal of a nasal polyp, which by continuous mechanical irritation had doubtless given rise to the condition underlying. Examinations of the nares of

hay-fever patients have repeatedly failed to show any local disturbance other than general congestions. Daly's theory was subsequently accepted and supported by Hack and Roe, who both affirmed that the influence of a morbid condition of the nasal mucous membranes favored the development of hay-fever. In 1883 Sajous and Herzog wrote important papers to prove the same facts. In 1884 J. N. Mackenzie demonstrated that "there exists in the nose a well-defined sensitive area whose stimulation through a local pathologic process, or through an extra irritation, is capable of producing an excitation which finds its expression in a reflex act or in a series of reflected phenomena." He located this area at the posterior end of the inferior turbinated bones and corresponding portion of the septum. It has since been held by advocates of the local

theory, that diseases and abnormalities of the nose, such as a markedly deviated septum, outgrowths from the septum, hypertrophic rhinitis, enlargement of the inferior or middle turbinated bodies, mucous polypi, and marked turgescence of cavernous tissue on the inferior turbinated body, were all provocative of hay-fever paroxysms.

In 1884, Harrison Allen declared that the primary lesion was one of obstruction, temporary or permanent, in one or both nostrils, from one of various causes, attended by vascular dilatation. Bosworth likewise held that the existing morbid condition of the intranasal tissues must be one of an obstructive character, tending to produce in itself vascular dilatation. Regarding nasal polypi, occasionally considered as active causes of hay-fever, Bosworth concludes that they are rather a result

than a cause, since the great quantity of outpoured serum makes the nasal mucous membrane sodden or water-soaked, and in this way myxomatous degeneration develops, eventually assuming the form of polypi.

J. N. Mackenzie, however, examined the nares of many sufferers from hay-fever without finding any nasal lesion. Holmes noted an instance most carefully reported, in which, with cold snare and galvanocautery, all obstructions were removed, and areas rendered anesthetic so that a probe no longer excited reflex symptoms, yet the patient suffered from hay-fever with scarcely diminished intensity. He further observes that at least a degree of the condition might be the result and not the cause, the peripheral susceptibility being an outward expression of an inward state.

In 1885, Thornwaldt, in Wiesbaden, in

his observations on nasal catarrh, assumed that nasopharyngeal disease might not only give rise to symptoms simulating nasal disease, but was likely the actively predisposing cause of asthma and hay-fever. Bosworth agreed with him as far as hay-fever is concerned.

In 1893 Seth S. Bishop announced to the American Medical Association that "an excess of uric acid in the blood causes hay-fever, or nervous catarrh." Uric acid in the blood in marked excess of the normal relation to urea, of about one to thirty-three, causes certain disturbances of a vascular and neurotic character. In health, five to eight grains of uric acid are secreted every twenty-four hours. Haig claimed that an effect of an excess of uric acid is contraction of the arterioles and capillaries all over the body. He found that by diminishing the alkalinity of the

blood it was freed from uric acid, the arterioles were relaxed, and the headaches and mental depression were relieved. Cerebral anemia has appeared to obtain in hay-fever, and the attacks were relieved, Haig found, by such remedies as relieved anemia of the brain, *e.g.*, amyl nitrite, coffee, and other cerebral stimulants. These views of Haig were concurred in by Thomas J. Mays, Murchison, Conklin, Ebstein, Quinquaud, and others. Bishop, in 1894, remarked that the blood in the morning is more alkaline than at any other time of the day, being, at about nine o'clock, at its greatest point of alkalinity, which would seem to account for those attacks of hay-fever which came on early in the morning, and which in some instances were ascribed to the influence of light. He was of the opinion that not only an excess of uric acid in the system, but also an increased

formation thereof should be regarded in the treatment of hay-fever. Bishop also claimed that the uric-acid theory was not antagonistic to the essentially neurotic character of the disease. He also advanced that the primary determining cause of the particular manifestations in this disease is an inherent, perhaps hereditary, susceptibility of the nervous system. In this way only can we account for the fact that the same subjective or objective exciting cause (uric acid or pollen) will produce one train of distressing symptoms (nervous coryza) in one individual, and an entirely different one in another (asthma). This uric-acid hypothesis explains why some persons suffer from attacks under certain conditions in winter as well as during the warm months. It also unifies all the forms.

Bishop says: "The uric-acid theory of

hay-fever is not antagonistic to the present status of medical opinion or surgical treatment, but, on the contrary, it explains questions that were inexplicable before. As a tumor or hypertrophied bone may give rise to convulsive seizures in epilepsy, and as its removal may be followed by relief when no other structural cause exists, so in hay-fever, when new growths and other lesions of the nasal mucous membrane are present, the attack may be started by the accumulation and the sudden setting free of uric acid. This precipitates the paroxysm by its irritant action, which finds expression in the group of symptoms characteristic of hay-fever or asthma, instead of some one of the other allied diseases. The particular form of manifestation may be determined by the growth or the seat of irritation located in the nasal cavities. When this is the only de-

termining factor of the nature of the morbid symptoms, no other disease having resulted from the long-standing trouble, the removal of such a peripheral source of irritation may give relief from these symptoms, but it may not prevent the uricacidemia from switching off into other kindred lines of disturbances, if it be not corrected."

Capp, in advancing a new theory, inclines to the uric-acid theory, and alludes to a certain spastic condition not mentioned by other writers, which, altho slight in character, is general, rather than confined to limited areas, and in a large measure accounts for many manifestations of the disease. A central nervous irritation is probably caused by the presence of a disturbing element in the blood, presumably products of imperfect metabolism not eliminated. This may originate nerve-cur-

rents with innumerable reflexes, which, in the disturbed equilibrium of the system, are, in a measure, uncontrolled by the ordinary inhibition.

Holmes has very cleverly pointed out a fallacy in regard to the evidence advanced to substantiate the uric-acid theory. He states that some investigators by the use of salicylic acid and various acids to diminish the alkalinity of the blood, thus eliminating uric acid, have, thereby, actually aggravated the condition in hay-fever, which aggravation has been thought due to excess of uric acid in the tissues, or increase in its production, instead of being due to the idiosyncrasy to salicylic acid, etc.

In 1897, Grayson stated that even if we grant that a certain number of hay-fever patients are unquestionably people of a neurotic temperament, while others are

gouty, can not we profitably look beneath these titles and recognize the fact that they are dyscrasies, which are merely different offshoots from a parent weed that is rooted in defective nutrition? By defective nutrition is meant all the phenomena of metabolism,—constructive, destructive, and eliminative. Disturbance of one means disturbance of all. With continued absorption of toxic materials from the intestinal tube, or with persistent incomplete elimination of the products of suboxidation, it is only a question of time when autotoxemia will provide us with any of the functional neuroses from hay-fever and asthma to chorea and epilepsy.

Grayson says the neurotic habit may exist, but it is not essential to the disease, but the nervous system is implicated as a victim, not as a culprit. He claims that hay-fever is a defect, not of the nervous, but of

the nutritive system, because impairment of the digestive and nutritive processes is almost invariably the first downward step toward a general state of lowered vitality. At first gastric, it later involves the whole gastro-intestinal tract. He thinks uric acid is almost invariably present in excess in hay-fever subjects. A child having reflex convulsions due to acute indigestion is not a neurotic subject, yet the vasomotor perturbation of the hay-fever patient differs from that of the child mainly in point of chronicity.

Grayson concludes that the three factors which make up the etiologic combination of hay-fever are: An external irritant, some intranasal abnormality, and a constitutional element—"defective nutrition." The physician unaided can not restore the nose to a state of health. In order to overcome the self-indulgence of the patient,

regularity is recommended in eating, work, and play, while indiscretions of diet, lack of exercise, objectionable fancies in matters of clothing and bathing, and, finally, vicious excesses—alcoholic, narcotic, or sexual—will require the constant and most determined effort of the patient himself. The whole environment of the patient must be separately studied and provided for in the dietary scheme. A comment on this treatment is: "While it is true that if a man takes care of his muscles his nerves will take care of themselves, there is no closing of the eyes to the fact that to the average man exercise is distasteful; therefore, it is the more necessary to be explicit in instructions concerning it. Altho there is nothing brilliant about this method of removing the constitutional factor of the disease, what it lacks in brilliancy is more than made up in certainty, and if the

patient is possest of grit and determination it brings a sure reward."

J. Müller thinks there is a causal relation between hay-fever and gastro-intestinal symptoms, but he also holds that it can be proved that pollen entering the respiratory tract is the cause of the disease. A "sufferer," writing on the disease, says: "Indigestion is a most potent cause in many instances, and proper food, properly digested and assimilated, has permanently relieved more than one." But he does not say he himself was relieved, nor does he give cases.

It is questionable whether or not the digestive disturbances are not effects rather than causes of the disease. It is not at all doubtful, however, that lowered resistance and a depreciated vitality may result from difficulty in the gastro-intestinal tract. Such difficulty may suffice to start the chain of hay-fever symptoms.

PART III

FORMS OF TREATMENT

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1. Preventive Measures

In the young we find preventive treatment giving the greatest rewards. This calls for careful attention to the general health of the growing child. The medical profession has done much to awaken an interest in preventive measures among parents, and in no way has the family physician reduced infection more thoroughly than by insisting on a careful toilet of the nose and throat. In this way he has very frequently prevented many of the more serious diseases of the growing child. Personal hygiene is as valuable as domiciliary hygiene, yet, if either is neglected disease is certain to continue.

The careful parent will insist upon frequent professional examinations of his children and at the first sign of discomfort have any abnormal condition corrected. It is not wise to wait until distress compels relief, and if hay-fever is an inheritance in a family it is especially important. Children with enlarged tonsils and adenoids should have them removed not only to in-

crease their mental poise but to secure their physical comfort, and also as a step in escaping hay-fever. Adenoids are frequently the cause of broken rest at night, with earache, a tendency to repeated bronchitis; this is seen more frequently during spring and fall. This condition may bring on change in voice and ofttimes a running nose. With enlarged tonsils we frequently encounter the unproductive cough. We may mention, while passing, that enlarged tonsils remaining after the tenth year should be removed, as they are undoubtedly hopelessly diseased. I am a firm believer that tonsils and adenoids should be removed early, for, in addition to this local discomfort, they influence the mental health by rendering possible a more systemic depreciation of the child. The frontal sinus may become involved as well as the ethmoid. Young children are frequently found to suffer with deviated septum and this contributes to the general discomfort. With the pressure of retained secretion polypi are not unusual.

Ballinger has been imprest with the possible relationship of catarrhal sinusitis, particularly ethmoidal and frontal, to hay-fever. He has found surgical treatment of the sinusitis to be followed by relief of the hay-fever. The difficulty in the way of diagnosticating catarrhal sinusitis has been so great that it has been frequently unrecognized. Hay-fever due to catarrhal sinusitis has been cured by Dr. P. M. Farrington, of Memphis, by the use of autogenous vaccine.

Dr. Ballinger quotes the late Dr. Schadle, who called attention to the possibility of relationship between maxillary sinusitis and hay-fever. Whether or not such a relation exists, we must recognize the fact that the local hyperesthesia probably has an anatomical or inflammatory origin. The hypersensitiveness does not "happen" but has a definite cause. The hypothesis is still further supported by clinical facts—that some cases of hay-fever are cured by successful treatment of the sinusitis. Heredity may impress a neurotic temperament on the growing child with tendency to gout or rheumatism. This unstable condition of the nervous system is difficult to define, there may be an excess or decrease in the nervous energy. There may be a faulty metabolism whereby certain toxic substances are liberated in the blood current. That hay-fever subjects are usually neurotic has been generally accepted. Why they are neurotic is a much mooted question, concerning which ingenious theories have been advanced, but none of which are convincing.

Preventive treatment for hay-fever, therefore, must take in family history and family tendency in an endeavor to correct local, as well as constitutional faults. This intimate knowledge of family history gives the physician the insight to the constitution of the child. Heredity may do much to balance or unbalance nervous energy, it may do more to handicap a child physically, but I am of the opinion that environment plays a most important rôle in the growing child. In

childhood preventive measures yield the best returns, and this is well illustrated in the development of hay-fever tendency, and it is wise that the masses have grown active to the needs of the young.

As an important feature in preventive measures I can do no better than quote here the article of Dr. Scheppegrell, the president of the American Hay-Fever Prevention Association, on "Hay-Fever; Its Cause and Prevention."[1]

"From the standpoint of the number of patients affected, hay-fever ranks among the first of the non-fatal diseases. While accurate statistics regarding the number of patients are not available, a conservative estimate has placed the number of persons in New Orleans affected with hay-fever at not less than 3,500, or one per cent. of the total population. Hay-fever is prevalent in the greater portion of the United States, and the proportion in New Orleans is a fair average of its prevalence in other sections. The total number of those suffering from this disease, therefore, is so large that the subject demands the most careful consideration.

"In spite of the greater increase in medical knowledge, many cases of hay-fever are still mistaken for ordinary colds. The symptoms described and their recurrence at certain periods of the year should simplify the diagnosis. In doubtful cases this may be confirmed by testing

[1]Published in the Journal of the American Medical Association for March 4, 1916.

the patient with a small amount of pollen.

"Some of the staminate flowers of the suspected plant are placed in a small sterile gauze-bag, and this gently sniffed by the patient. In susceptible subjects this is quickly followed by a slight reaction. The patient may also be tested by approaching the suspected weeds so that some of the pollen is inhaled in this way.

"In the majority of cases, however, these tests are unnecessary and should ordinarily be avoided on account of the danger of developing a latent pollinosis. The beginning and end of the attacks are usually found to be coincident with the pollinating period of certain plants with wind-borne pollen, which, with the symptoms described above, is sufficient to confirm the diagnosis.

"Some physicians still believe that hay-fever is a local manifestation of some constitutional condition, in spite of the fact that the majority of patients, with similar conditions, have no such manifestations, and that when the pollen is not present, as on a sea trip, they do not occur. Improved education in the etiology of this disease, and more careful observation, will gradually correct this error.

"Even had therapeutic measures been more successful, prophylaxis, based on the removal of the exciting cause, should have been advocated as in malarial and typhoid fevers, tuberculosis and other diseases of known cause. Hay-fever, however, has been the stepchild of preventive medicine, and until recently no organ-

ized efforts in this direction have been undertaken.

"In view of the great and increasing number of hay-fever patients, their prolonged distress, the unsuccessful results of all curative measures and the distinctive preventable character of the disease, the American Hay-Fever Prevention Association has undertaken a campaign of education, to be followed in due time by suitable legislation, for the prevention of hay-fever.

"In the educational part of this work, the first consideration is the correct diagnosis of hay-fever and the acceptance of the fact that all cases of true hay-fever are the results of pollen inhalation.

"The identification of the various weeds and plants that may develop hay-fever is of the utmost importance, but will gradually follow the establishing of the etiology of pollinosis. As these principles become better understood, the physician, when consulted by a patient with hay-fever, instead of limiting his attention to writing a prescription or injecting a vaccine, will investigate the presence of hay-fever-producing weeds in the neighborhood of the patient's residence or vocation. In many cases the eradication or even the cutting of such weeds produces immediate results.

"In one of my patients, the offending weed, *Ambrosia artemisiaefolia* [ragweed] was growing in his garden. In another, a school-teacher, affected with hay-fever for many years, on being questioned stated that there was an abundance

of flowering weeds in the vacant lots adjoining her house. When specimens of these weeds were produced they were found to be the *Parthenium hysterophorous,* one of the causes of hay-fever in south Louisiana. In both of these cases marked relief soon followed the cutting of these weeds. In order to obtain complete relief in such cases, however, the cutting of the weeds should be over a considerable adjoining area, as the pollen is wind-borne to a distance depending on the velocity of the wind.

"While the removal of the offending weed is the correct measure, relief may also be obtained, when this is impracticable, by avoiding the proximity of weeds known to be toxic to the patients. In many cases this is entirely practicable, as shown in the following case in which the attack was postponed for thirty-three days:

"E. G., manager of a sugar plantation near New Orleans, has been a sufferer from hay-fever for the past ten years, the attacks always commencing about August 25th. After the influence of the ragweed to this form of hay-fever had been explained to him, he concluded that his attacks were due to the pollen of the trifida ragweed which grows on a road some distance from his residence. He, therefore, avoided the road, and until September 28th, for the first time in ten years, he had had no attack. On this date he found it necessary to pass this road. In twenty minutes he commenced to sneeze, that night he had a violent attack, and the following day he had his usual annual hay-fever.

"The treatment of cases by the eradication of the hay-fever-producing weeds will not only produce direct results, but will also prove a powerful impetus in educating the public in the relationship of such weeds to hay-fever. It will result, moreover, in having these weeds considered from a new point of view. Instead of simply indicating neglect or careless cultivation, they will be looked on as a source of disease and discomfort to a large class of sufferers. This will not only bring the leverage of public opinion to the eradication of these weeds, but will eventually simplify the question of legislation.

"In connection with the question of public education, the American Hay-Fever Prevention Association has received a communication from Dr. Rupert Blue, surgeon-general of the United States Public Health Service, and one of the honorary vice-presidents of our association, in which he summarizes this in a very concise manner:

" 'It appears that the most practical method of securing the cooperation of the public would be by education as to the effect of the presence of these weeds in communities from both health and economic standpoints. This seems to be the primary object of your association, which is to be commended for its efforts.'

"Some of the early forms of hay-fever are due to the pollen of the *Graminaceae* or grasses, which include the cultivated varieties, such as rye, wheat, corn, etc. These form a common cause of hay-fever in England and on the Conti-

nent, where the autumnal form due to the ragweed is not found, owing to the absence of the weed.

"While this is of much less frequency than the fall hay-fever in the United States, it represents in the aggregate a considerable number. When these cases are due to the cultivated varieties, the knowledge of this fact should induce the patient, whenever possible, to live away from such cultivated fields or at least to avoid them during the active season of pollination. Only in those cases in which the removal of the offending plant is impossible will the question of treatment be given preference over prevention.

"As the autumnal hay-fever is the most prevalent form in the United States, and, in the majority of cases, is due to ragweed, the American Hay-Fever Prevention Association has given its first attention to the eradication of this weed. The description and illustration of both varieties (*Ambrosia artemisiaefolia* and *trifida*) have been sent to the State boards of health of each State and of the District of Columbia. Many of these have published the cuts and descriptions, and a number have sent them to the newspapers of their State for publication.

"The United States Department of Agriculture has assisted and is furnishing valuable information for this work. Arrangements have been made with the Hygienic Laboratory of the Public Health Service at Washington to make investigations on the hay-fever pollens submitted by our research department. Encouragement

or promise of active cooperation has been offered by the majority of the State boards of health, these being as follows: Arkansas, Alabama, Arizona, California, Colorado, Delaware, Florida, Idaho, Indiana, Iowa, Kansas, Kentucky, Louisiana, Massachusetts, Michigan, Minnesota, Nevada, New Hampshire, New Jersey, New York, North Carolina, Oregon, Tennessee, Utah, Virginia, Washington, West Virginia, Wisconsin and Wyoming.

"The common ragweed (*Ambrosia artemisiaefolia*), while found in great abundance, presents no special difficulty in eradication, as it is an annual and reproduced only by seed. In carefully cultivated lands it is not found in appreciable quantities. Where the land is not cultivated this weed may be entirely kept down by grazing cattle. When, however, it has been neglected, the weed should be mowed before the latter part of August, in order to prevent pollination.

"The giant ragweed (*Ambrosia trifida*), which grows in similar abundance in the moist lands of the coast, presents a more difficult problem, as the roots are perennial. Until this weed is two feet in height cattle will feed on it with avidity, which will probably prove useful in destroying it. In carefully cultivated lands it is rarely found. The question of the best scientific method of eradication of both the ragweeds has been referred to the United States Department of Agriculture, and the results of this investigation will be reported later.

TALL WORMWOOD

GREAT RAGWEED

"With a view of showing what can be accomplished by organized efforts in the prevention of hay-fever, the American Hay-Fever Prevention Association has concentrated its first efforts in New Orleans in the following manner:

"The public was first educated regarding the ragweeds, so that they could be easily recognized. Illustrations of the weeds were published in the Bulletin of the State Medical Board of Health and the public press, and the live weeds, in full development, were exhibited in a show-window of the principal street.

"The city of New Orleans, through the commissioner of public works, placed at the disposal of the association twenty convicts, who cleared the streets and sidewalks of the outer sections of the city of the weeds, in accordance with a map prepared by the topographic committee of the association, showing the areas infected with ragweed. The city board of health assisted by enforcing the cutting of weeds in vacant lots and the commissioners of the various parks had the ragweed destroyed in the public parks under the direction of the association.

"Valuable assistance was given by the Women's Civic League, which appointed a special committee on vacant lots. This committee made arrangements with labor bureaus so that it not only reported lots infected with weeds, but offered to send workmen to cut them at low rates.

"The storm of September 29 destroyed practically all the leaves and flowers of the remaining giant ragweed in exposed places. As a

result of this, and the efforts of the American Hay-Fever Prevention Association, fall hay-fever practically disappeared in New Orleans several weeks earlier than the usual time. This campaign will be resumed next spring, when its management will be placed in the hands of the State Hay-Fever Association.

"The American Hay-Fever Prevention Association believes that what has been effected in New Orleans can be done in all towns and cities. In some of the smaller towns, especially those catering to summer visitors, this could be accomplished before next summer. The statement that a town is free of hay-fever will prove an advertisement that will easily repay the cost of destroying the hay-fever-producing weeds."

2. Local Treatment by Nasal Applications

Local treatment of hay-fever has been viewed with diverse opinions by every writer on the subject. Many good authorities condemn all internasal treatment as useless and irritating, while others strongly advocate its value. It needs no argument to show the value of nasal and throat applications of antiseptic nature in the early stages of influenza or any other neutral catarrhal irritation of the eye, nose or throat. Indeed many household epidemics have been shortened or aborted by the careful attention to these parts. I am not alone in the state-

ment that severe household epidemics have been deprived of their danger by careful cleansing of the nasal mucous membrane before the infection became systemic. Indeed, this is the routine treatment in every well-regulated family where children are found, especially during winter and spring, and in the early fall. It is much more important that this should be carefully observed if the neighborhood is infested with an epidemic of catarrhal colds. The repeated infection of some families and the escape of others is not so much in the vital resistance of the several members, but the neglect in the individual of personal hygiene. This is true of all diseases, as well as of hay-fever. It is true that children, and young people in general, are more likely to contract catarrhal colds if they are burdened with adenoids or hypertrophied tonsils — diseased by repeated former attacks. I believe that the acute infectious diseases, particularly in children, may be lessened by most thorough and repeated sterilization of the nasopharynx, and just as house epidemics are never excusable evils so I claim the same to be eventually true of hay-fever.

The important result to be obtained through local treatment is the prevention of the paroxysms, and, ultimately, the removal of the recurring habit periods; *i. e.*, the destruction, if possible, of the recurring habit. Years ago I was led to treat my hay-fever patients by cleansing the nasopharynx with an atomizer containing a warm solution of boric acid (ten grains to an

ounce of water) or Dobell's solution, after which I carefully wiped the mucous membrane and applied menthol and camphor and liquid cosmoline freely to the parts. This procedure afforded considerable temporary relief in a large number of cases when there was present simply turgescence of the whole nasopharynx.

℞. Sodium bicarbonate,
Sodium borate ....āā ℥iss
Carbolic acid .... ʒj.
Gylcerin .... ℥ij.
Rose water (25 per cent.)............q.s. Oj.
SIG.—Teaspoonful to one ounce of warm water.

This I thoroughly use in both nostrils, first by means of an atomizer, after which, with a curved applicator or cotton-carrier, I very carefully swab the whole nasopharynx. I scrub most carefully and gently every portion of the mucous membrane, being sure to reach between the turbinated bones and all around and over every slight prominence. I then as carefully dry the membrane with clean cotton, and use freely a mild solution of menthol and camphor in albolin, in proportion as follows:

℞ Menthol .... gr. v.
Pulverized camphor .... gr. v.
Albolin .... ℥ij.

I loosely plug the nose for a few minutes to retain the oily application. It is important to sterilize most thoroughly the sensitive areas

of the nose, as we are unable to determine whether one or more may be affected, and by this mild yet thorough treatment we cleanse effectually the whole nasal chamber.

This treatment was so extremely simple that for a long time I doubted its real value, but as so many sufferers have exprest their relief, and were willing and anxious for me to continue the applications, I have concluded to offer my methods in full confidence of their usefulness, with a warning that for successful treatment the instructions for cleansing and scrubbing must be followed in careful detail. Good results need not be expected by simple irrigation and swabbing—the whole nasal mucous membrane must be *thoroughly washed* and *gently scrubbed* before the oily applications are used.

This internasal treatment should commence *four* weeks before the expected onset of the paroxysm, and should be done daily, if possible.

I have found many persons who will not tolerate the use of carbolic acid, even in so mild a solution as that given above, the weakest solution frequently causing a severe urticaria.

When various idiosyncrasies to carbolic acid forbid its use, I select as the second best detergent hydrogen dioxid, and commence with the following mixture:

℞ Hydrogen dioxid,
Glycerin .... āā ℥ss.
Distilled water .... q.s. ℥iv

With this I spray the nose most thoroughly, following it up with plain warm normal salt to remove the accumulation of foam that will necessarily collect in the nasal spaces. A few days, or, better, one week prior to the date of the onset, I increase the strength of the hydrogen dioxid solution, using something like the following:

℞. Hydrogen dioxid .... ℥ij.
Glycerin,
Distilled water ....āā ℥ij.

This must be removed also by means of the normal salt, as already mentioned. In a number of cases I have found glycerin objectionable as a vehicle, producing an irritation of much annoyance. In such cases I omit the glycerin and substitute normal salt. In a few cases, the hydrogen dioxid produced an inflammation of the mucous membrane that would require its dilution. We find many personal idiosyncrasies in a large number of hay-fever sufferers that one might go on indefinitely with modifications of treatment, but, as in general practise, it is our aim to treat the individual primarily, and we can not dogmatically hold fast to any special drugs or formula.

In the few obstinate cases in which sterilization seems to provoke trouble, and the slightest manipulations of the nose and throat precipitate violent paroxysms, I use the following:

℞. Morphia Muriate .... gr. i
Menthol pulv. .... gr. ii
Boric acid .... gr. x
Camphor pulv. .... gr. xii
Starch pulv. .... z. iv mft.
SIG.—Use as a snuff, frequently.

The following to be taken internally:

℞. Tablet Suprarenal Ex................. gr. v.
SIG.—One every three or four hours.

Many physicians claim that relief can not be afforded to hay-fever patients without using cocain or eucain at some time during the management of troublesome cases. It is very exceptionally that I resort to either; possibly an unusual case will require one or more applications to control a local storm, yet the majority of patients never receive cocain from my hand.

In severe cases that came under my care after the disease had been well established, when I had no chance to conduct a preliminary course of benumbing, I have been forced to prescribe something like the following:

Menthol .... gr. viij.
Boric acid .... gr. xxx.
Albolin .... ℥ij
Solution of Eucain "B" (4 per cent.).... ℥ij

This is applied carefully and thoroughly on cotton applicators to the mucous membrane of the nasopharynx. It may control the attacks, and it frequently aborts them and keeps the

patient decidedly comfortable. I have found the direct application of the remedy more satisfactory than the atomizer. In some cases, for a few days, this application must be made two or three times daily.

H. L. Swain recommends the local use of the aqueous extract of the suprarenal glands in certain chronic conditions of the hay-fever type, as a powerful local vaso-constrictor and contractor of erectile tissue. The local effect can apparently be obtained any number of times without entailing a vicious habit, such as might result from cocain. Ingals and Ohls report that they have obtained much relief in these cases by the use of an extract of suprarenal capsule prepared as follows: Adrenals (Armour's), ℥j; boric acid, gr. xvj; cinnamon water, ʒiv; hot camphor water, ℥j; hot distilled water, enough to make ℥ij. Mix, macerate for four hours, and filter. This solution remains stable for several weeks. It is used as a spray four or five times a day. I have not had occasion to resort to the local application of this substance, but I have had one patient who was distinctly benefited by internal administration in doses of gr. ¼ to gr. j, as often as four times a day. He was a catarrhal young man of neurotic temperament, who came to me during the first week of his attack, and who objected to the usual routine sterilization of the nasopharynx.[1]

[1]Personally the use of the suprarenal extract has been of little value owing to the violent sneezing provoked.

The formula:

Adrenal chlorid .... ʒij.
Normal salt sol. ....q.s. ℥j.

is more elegant and convenient.

3. As to Diet, Exercise and Rest

In old cases, when the nerve-habit has long been formed, treatment should commence at least two or, better, three weeks before the anticipated recurrence of the paroxysms. All bodily irregularities must be corrected and tendencies to constipation or dyspepsia removed. Amylaceous indigestion should be corrected by the exclusion from the dietary of too starchy foods. For the elimination of excessive uric acid, or other waste products, and to relieve constipation, the systematic administration, morning and night, of sodium phosphate, is invaluable. If the appetite is not good, the regular use of the tincture of nux vomica, ten to twenty drops three times a day, is strongly indicated. In anemic cases pills of carbonate of iron or, probably still better, the pills of valerianate of quinin, iron, and zinc are necessary. In nervous cases with anemia, valerianate of zinc, one grain, with two grains of the compound asafetida pill, two or three times a day (after Morell Mackenzie), will be found valuable. Careful diet, a tranquil mind, and moderate exercise are essential. Outdoor exercise, with a

daily tepid bath followed by vigorous friction of the whole body, will help to eliminate waste material. The patient should not unnecessarily expose himself to direct rays of the sun, as they are calculated to excite intense reflex irritation of the sensitive nerve centers. Much trouble may be averted by the use of a sunshade or umbrella and by the avoidance of exercise in the sun.

It must be understood that with the general hygienic and constitutional treatment the course of local prophylaxis by daily sterilization is most necessary.

The treatment of neurasthenic cases, or those in which a decided derangement of the general system as well as of the nervous energy exists prior to the attack, requires the greatest tact and skill. If there is little local catarrhal disturbance there will be great difficulty in combating the disease in the face of the deprest vitality and lessened nervous resistance. In such cases I place the patients upon a diet, somewhat like that in the appended list, and urge strict adherence to it. After obtaining careful urinary analysis and other clinical data, I often further specialize in the diet, or I may increase the variety according to the needs of the individual. In these cases I always urge the drinking of large quantities of water, unless there is some strong contraindication. Neurasthenics will often avoid water between meals. I at once order systematic massage. If the patient does not care for a masseur, I order a daily tepid bath of a

temperature between 80° and 85° F., with a coarse towel rubbing, followed by a douche of cold water along the spine. This should be continued for at least two weeks prior to the onset of the paroxysms.

Rest for the overtaxed function is imperatively demanded. Unfortunately, this is more easily prescribed than carried out. In wealthy patients the Weir-Mitchell rest-cure often gives brilliant results. In other cases a change of scene and a temporary rest from business or society may be accepted when the sanitarium would be out of the question. Quiet resorts on the sea coast or in the mountains are desirable. Nothing is better than two or three weeks on the ocean. A compromise may be obtained by having the patient give up a portion of the daily duties and go to bed earlier at night. The patients should not be allowed to discuss their ailments too freely. Horseback riding, bicycling, rowing, and walking—in fact, any outdoor diversion not too violent—are to be recommended.

If the patient suffers from insomnia, careful administration of a hypnotic may help to reestablish the sleep-habit. At first give a warm bath, and a glass of warm milk or malted milk before retiring. If this and other similar measures do not avail, five grains of Veronal capsule may be given one hour before going to bed. If the patient is accustomed to awake after a short sleep, the Veronal should be given at bedtime. Full amounts of sleep are neces-

sary to neurasthenics. Depressants, such as the bromids, chloral, and the opiates should be avoided. Any coexistent gastric or cardiac trouble must be carefully treated, and the bowels kept open regularly.

The diet that I find most desirable to follow, generally speaking, is that which is applicable to the gouty or uric acid diathesis.

General Rules.—The diet should be liberal, but not stimulating, with moderation in animal foods and very little of foods having a tendency to produce acids in the system, such as starches, sugars, fats, and fermented liquors. Patients may take soups—clear or vegetable—and weak beef tea or broths.

Fish.—Fresh fish and raw oysters.

Meats.—To be taken once a day only—mutton, chicken, underdone roast, sweetbread.

Eggs.—Moderation. White of eggs, raw, or shirred in drinks, such as lemonade, occasionally.

Farinaceous.—In small quantities. Toast, stale bread, bread from whole wheat, rye bread, milk toast, rice, crackers.

Vegetables.—Fresh, green varieties preferable; celery, lettuce, watercress, cucumbers, onions, cabbage, salads, sparingly of baked potatoes, young peas, string beans, and spinach.

Desserts.—Oranges, lemons, apples, apricots, pears, peaches, cherries, blanc-mange (not after meals, however), stewed fruit.

Beverages.—Water, plentifully, especially before meals; plain soda, milk, buttermilk, weak

tea or coffee (without sugar), toast-water, lemonade. Mineral waters, such as Saratoga Vichy, Berkeley (Hot Springs), Lithia Water, Carlsbad, and Crab Orchard.

Stimulants.—Light Hock; Bordeaux in small quantities and well diluted.

Articles Forbidden.—Patients must avoid rich soups, hard-boiled eggs, fried and made dishes of all kinds, entrées, pickles, spices, veal, pork, duck, goose, salmon, lobster, crab; preserved, dried, and salted meats; salt fish, pickled pork, asparagus, old peas, beans, tomatoes, mushrooms, truffles, dried fruit, preserves, pies, pastry, rich puddings, patties, new bread, cheese, sweets, malts, sweet wines, strawberries, rhubarb, cider, fermented drinks, beer.

4. When Asthma Occurs as a Sequel

About five to ten per cent. of my whole number of hay-fever patients have suffered more or less from asthma. Asthma, as a sequel in these cases, manifests itself about the end of one week or ten days after the expected paroxysms of hay-fever, and is induced usually by some undue exposure or a damp or rainy day. My asthmatic patients, I find, were among those irregular in treatment, or those who had first called late in the disease. In these cases much mucous had accumulated in the larger tubes. If I can not clear the bronchial tubes by an emetic dose of ipecac, I prescribe somewhat as follows:

Potassium iodid .... ʒss
Ammonium muriate .... ʒss
Sirup of Yerba Santa .... ℥j.

A teaspoonful administered every two hours generally brings relief. A number of asthmatic patients require a solution of nitrogylcerin, one per cent. Of this, one drop every two hours for two or three days is given. Occasionally it seems imperative to give morphin. Some of my asthmatics have informed me that they can bring about immediate relief by plunging both hands in hot water and taking a drink of whiskey, followed by a large draft of hot water. It is possible for some persons to voluntarily combat their asthmatic attacks, and for this reason they should be encouraged to practise certain breathing exercises until they can in a measure control their respiratory apparatus. Asthmatics usually have, however, a preexistent catarrhal state of the bronchial tubes, which exhibit marked vasomotor changes on slight irritation. If I see these patients early, I prescribe five-minim capsules of the oil of sandalwood four times a day, or the compound salol capsule, and by the time their period arrives, the bronchitis is fairly well cleared up.

The inhalation of the fumes of burning niter-paper or specially prepared powders, or of cigarets, gives relief in many cases. The powders used at the Brompton Hospital by Sidney Martin contain one part each of anise and niter, two parts of stramonium leaves, and five grains

of tobacco to the ounce; one teaspoonful is to be burnt on a plate and the fumes inhaled. A pill containing 1/4 of a grain of morphin, with 1/200 of a grain of atropin sulfate, given at bedtime, is sometimes useful in connection with the inhalations. Extract of stramonium (1-16 of a grain) may be substituted for the atropin.

Van Sweringen calls attention to a line of treatment in a very obstinate case of bronchial asthma that was attended by remarkable results. The attack had lasted for two weeks, during which time all the antispasmodics had in turn been exhausted, and the patient had secured but a period of two hours' freedom at any one time. Finally, based on the theory that if asthma was a reflex it must be under the control of Setschenow's inhibitory center, and that anything that would stimulate the inhibitory center would lessen the reflex-spasm, quinin and strychnin were given, with excellent results. The dose of the quinin was seven grains. The extract of nux vomica was given in 3/4-grain doses, and to this was added 1/4 of a grain of codein sulfate. In the interval the iodids were continued.

However, the use of sedatives and inhalations must be limited, especially in the milder and uncomplicated forms of asthma, while efforts to benefit the patient's general condition are strongly indicated. Diet is an important part of the treatment of many cases. Not all cases of asthma are due to uricacidemia, but nearly all cases are benefited by attention to the diet and elimination of excess uric acid.

Of remedies that may be continuously administered to patients who have frequently recurring attacks, two are most constantly used—namely, iodid of potassium and arsenic. The iodid may be most conveniently given with stramonium, as in the mixture devised by Martin, which consists of 1/4 of a grain of extract of stramonium, two grains of extract of licorice, three grains of iodid of potassium, and five minims of chloric ether. This mixture may be given two or three times daily in cases of asthma. It possesses two disadvantages, however. The stramonium leads, in some cases, to paralysis of accommodation, but by diminishing the dose, the patient soon ceases to experience discomfort from the remedy. If given alone, the iodid must be administered in five-grain doses two or three times daily, the medicine being discontinued from time to time. Arsenic by itself, in doses of three minims of the liquor arsenicalis, is a useful remedy for continuous administration in asthma, and it may be combined with potassium iodid (three to five grains) in a mixture. Hydrotherapeutic treatment is of use in some cases of asthma. The patient should be accustomed to gradually colder baths of short duration, with douches.

5. The Use of Serums—Dunbar's Serum

The wide recognition of the serum treatment of hay-fever by Dunbar, of Hamburg, Germany, requires me to quote sufficient of his writings that my readers may appreciate the value as

well as the limitations of his work. To very briefly summarize: Dunbar has prepared hay-fever *antitoxin* by inoculation of horses with the toxins derived from the albuminoid body found in the starch particles of the pollen. The serum obtained from the horse is dispensed either in a liquid or dry form, and is designed to be applied to the mucous membrane of the nose and the eye when required.

His serum has been named *Pollantin,* and two forms are on the market, one prepared from rye pollen, especially used for spring and summer hay-fever, or "rose-cold," and the other, prepared from ragweed pollen, designed as a remedy for hay-fever occurring in the late summer and fall. Dunbar thinks that hay-fever is the result of a specific poison found in pollens and is an albuminoid body—and his antitoxin is intended to inhibit, or immunize patients against the *pollen toxins* if used previous to the hay-fever season. Its use is also to palliate the symptoms in cases where the disorder has already made its appearance. *Pollantin* produces a sensation of relief and cool comfort when applied to the inflamed mucous membrane of the nose or eye. This comfort remains for some time, but the relief is variable.

In 1902, Prof. W. P. Dunbar published,[1] as an appendix to a presentation of the history of our knowledge of hay-fever, the opinion, based on experiment, that hay-fever is a disease caused

[1]Zur Ursache u. spezif. Heilung d. Heufiebers. Verlag Oldenbourg, München, 1903.

by a poison derived from plants. These toxic substances are found in the dust of the blossoms of certain plants. They are present in the albumin of the pollen and are septic in nature. According to this theory, it would be possible, by means of the isolated toxic albumin of the pollen, to determine whether or not a given disease was hay-fever. It was also hinted, and in a publication that shortly followed,[2] positively asserted, that it was possible to produce a specific anti-toxin by inoculating animals, *e.g.,* rabbits or horses, with the albumin of the pollen. It was possible with this antitoxin to neutralize the poison of the pollen in vitro so that the latter would no longer cause symptoms in hay-fever patients. It was also claimed that symptoms that had already set in could be overcome by the use of the specific antitoxin.

By means of this timely use of the antitoxin the outbreak of the hay-fever symptoms should be prevented. As a result of further investigation he was later able to prove definitely[3] that by the proper use of the antitoxin it would be possible to rid patients of their disposition to hay-fever, and to immunize them so they could dispense with the use of the antitoxin or any other therapeutic agent without having to fear further attacks.

[2]Zur Frage betreffend d. Aetiologie u. spezif. Therapie d. Heufiebers. Berl. klin. Woch., 1903, No. 24–26.

[3]Zur Ursache u. spezif. Heilung d. Heufiebers II. Deutsch. med Woch., 1911, No. 13.

Th. Albrecht, the secretary of the German Hay-Fever Association, designated the appearance of my first article as a turning-point in the history of hay-fever. Other colleagues viewed the results of Professor Dunbar's comprehensive work with less favor. There were indeed those who claimed that he had added nothing new to the subject. The opinions exprest by the laity were also widely different in character. Some were unable to express their thanks in terms sufficiently strong, others claimed that the specific treatment suggested by him was absolutely worthless. An American correspondent wrote to him: "Your stuff is not worth a tinker's dam." In the face of such divergent opinions it seems worth while to cast a glance backward over the decade that has passed, to determine what assertions were right and what opinions were incorrect.

Whether we are right in looking upon hay-fever as a product of our modern culture, appeared to Professor Dunbar to-day, even more than it did ten years ago, an open question. In the last ten years there has been much published concerning hay-fever, not only in the leading journals, but also in the lay journals.

In so far as the latter deals with his work, they had not had his cooperation, nor had they consulted his wishes. There are to-day many hay-fever patients who are absolutely in the dark as to the nature of their disease. Even in Hamburg, after a scientific exhibition at which his hay-fever material was shown, many adults

came to him with the request that he should determine whether or not they had hay-fever. He was even more surprized to learn that there are to-day physicians who either deny the existence of hay-fever or know nothing about it. In view of this obtuseness it seemed to him very bold to say that two hundred and fifty years ago there was no hay-fever, simply because we have no authentic and convincing records from that time. The disease may have been very widespread then. There was missing perhaps only the man to notice the periodicity of the disease, its dependence upon the seasons of the year, and to correctly correlate the facts and draw proper conclusions.

Until ten years before, Dr. Dunbar says no one had been able to offer a clear and convincing explanation of the cause or nature of hay-fever. This is clear from a perusal of the literature up to that time.

Dr. Dunbar, himself a sufferer from hay-fever, had the opportunity during many years to test the merits of the various hypotheses concerning the cause of the disease. He finally came to the conclusion that only the pollen theory could be right. In his monograph concerning hay-fever, which thus far I have given in his own language as above, he described the observations which forced him to accept this explanation. For many years the attempt to definitely prove the theory met with an obstacle which seemed insuperable, viz., the impossibility of getting pollen in a pure state. In view of the extremely simple method

of doing this, this fact appeared to him to-day a remarkable one. He felt constrained to offer the following explanation:

"Year after year I consulted with botanists as to the best method of getting pollen in large quantities. Various methods were suggested to me, among others that of spreading large cloths over the meadows. I also sucked up into bottles large quantities of air in the attempt to get pollen, and attempted many other things. None of these methods met with more than moderate success, until I finally hit upon the simple procedure of shaking blooming plants, for instance stocks of wheat, and catching the dust that was shaken out. I succeeded better later by taking the ears shortly before they began to bloom and putting the stocks in water in a warm place. In this way I was soon able to gather pollen in large quantities, and, more important still, to isolate the pollen grains of different plants, free from all contaminations, including micro-organisms.

"After having obtained in this way the pollen of rye, wheat and ray-grass pollen (*Lolium perenne*), I could at once begin to attempt the settlement of important questions. A minimal amount of the plant dust when introduced into my conjunctival sac, or my nasal passage, caused in a very short time most pronounced hay-fever symptoms. The same experiment on my laboratory assistant, who did not have hay-fever, had no effect at all. Within a few days I extended the scope of my experiments so as to

include two hay-fever patients, who happened to be working in our institution, as well as three other assistants who did not have hay-fever. The result was always the same. The hay-fever patients reacted just as I did. Those who had no hay-fever and served as controls were not at all affected by the introduction of the pollen. These experiments were repeated later on very many patients and people without hay-fever, invariably with the same results.

"The next important point that suggested itself to me was to determine whether or not this toxin was active at other times of the year than during the hay-fever period. Formerly, it had been urged against the pollen theory that with the same pollen which had been active during the hay-fever period, no results could be achieved at other times of the year. Thus, for instance, Sticker was of the opinion that Woodward had proved that pollen was inactive except during the hay-fever period. He, therefore, was forced to come to the conclusion that for the production of an attack there was necessary the disposition on the part of the individual and the season of the year. The nature of the action of the season of the year was explained by some authors as a sort of an "Unstimmung," a sort of spring revolution. This explanation appeared to me very doubtful, because of the fact that this process occurs in European patients in springtime; in most American patients, however, in the fall.

"My experiments on this subject resulted as follows: Pollen which had been carefully dried

soon after gathering was active later at any time of the year. Pollen, however, which I enclosed in bottles in its fresh condition underwent certain changes, characterized especially by the formation of a liquid.

"Pollen which had been spoiled in this way proved later to be inactive. I might add here that these observations explained the occurrence of sporadic cases of hay-fever in the winter time. Pollen which has found it way into a dry room can remain active until the winter season —indeed, for many years, as I have shown. One blossom which has remained for eleven years in the herbarium retained an undiminished activity. Pollen which, on the other hand, falls to the ground in the open air, is destroyed by the first following rain. The fact that the pollen is carried down out of the air by the rain clearly explains further the remissions on certain days which had hitherto been so difficult to understand. By means of the isolated pollen I had then met those requirements in my attempts at an etiologic explanation which I myself have considered necessary. The suspected agent, free from all impurities, when applied to a hay-fever patient, must produce hay-fever invariably, regardless of the season of the year. The same agent applied to a normal person must have no effect. These requirements had, I say, been met by experiment.

"The grass pollen is so small that a single one can not be seen with the naked eye, yet its structure and chemical composition are very compli-

cated. Many pollen grains are covered with hair-like prickles. Adherents of the pollen theory formerly believed that hay-fever was due to these prickles. They asserted that hay-fever patients were extremely sensitive to the mechanical stimulus of the prickles, and that normal individuals were resistant to their action. It is true that some of the pollen, which we formerly looked upon as the cause of hay-fever, had an uneven, prickly surface. Some of the first adherents of the pollen theory believe that those pollen especially were active whose blossoms had an intense odor. The disease was, accordingly, at that time widely called rose-fever, linden-fever, and so forth, instead of hay-fever. I was able to show that those pollen which most often cause hay-fever had a smooth surface. This is true of all grass pollen, of which I have examined thirty-two varieties. These have also no odor. The blossoming of the rose and of linden occurs at the same time as that of the grasses. In 1902 I was able to completely overthrow the belief in the activity of the linden. It happened that in that year the blossoming of the linden was delayed from three to seven weeks in our vicinity, that of the grasses occurring at the regular time. The season for hay-fever was probably over at the time that blossoming of the linden was at its height, and hay-fever patients were able to enjoy the odor of the linden without any ill effects. I can well understand the tenacity with which hay-fever patients cling to the belief that the dust of the rose and

linden causes their symptoms. I myself banned from my home every rose and other odorous blossom during the hay-fever period, and felt certain that my suffering was thereby diminished. The relief was not an imaginary one, but was due to the fact that at the same time I kept my windows carefully closed.

"At about the time of the blossoming of the grasses, the pine (*Pinus sylvestris*) also begins to blossom and produces such a plentiful dust that thick clouds of it can at times be seen. This is called sulfur rain. I proved, in spite of the opposition of many hay-fever patients that the dust of this blossom was also of no consequence.

"By such experiments as these and many others I was able to prove that only certain specific pollen could cause hay-fever. This was in direct opposition to Blackley's theory. Other pollen, including those possessing sharp prickles, were absolutely without effect.

"The theory as to emanations, odors, ethereal oils, and so forth, had still to be considered. On opening a vessel that contains much grass pollen one gets an odor much like that of honey, which proved to be without effect on hay-fever patients. The odor of the linden, as well as that of the harmless rose, was proved to be without effect. There was still to be considered the questions as to the action of the ethereal oils. An extract of the oily and waxy portions of the pollen, when applied to the conjunctiva and nasal mucous membranes in small amounts,

caused a burning sensation. This was quite different, however, from the peculiar sensation experienced by hay-fever patients, which is so distinctive that nothing can stimulate it. These extracts had more effect on normal persons than they had on hay-fever patients. The amount of these substances with which we come in contact in our ordinary walks is so small that they can surely not be responsible for any of our unpleasant sensations.

"Grass pollen is distinguished from that of other plants in a marked way by the small rods which it contains, which look just like bacteria. Patton, in 1877, had already called attention to these rods. He believed that after they left the pollen grains they possest a movement of their own, and he drew the conclusion that they constituted the active principle of the pollen. He asserted that by reason of their inherent motility they found their way into the mucous membrane and the circulation and thus caused the symptoms of hay-fever. For a time, I also believed that these small rods played some part in the production of hay-fever. I did not know then that they were composed solely of starch, but thought they contained albumin. After I was able to get hold of great quantities of grass pollen I was able to isolate these rods by means of repeated centrifugation and washing. I was then able to prove that they were absolutely innocuous to hay-fever patients.

"As a result of certain observations, to which I shall refer later, I was soon forced to the con-

clusion that the active principle of the toxin of hay-fever is an albuminous substance. The alcoholic precipitate from a saline extract of a comparatively small number of pollen grains had an intense action on hay-fever patients, but none on normal individuals. After I obtained large quantities of pollen I began my experiments with the isolated albumin. Against this method of procedure it was claimed that I had not been working with a true hay-fever toxin, but with a denatured poison. For this claim there is no evidence; the critics failed completely to show any proof for the correctness of their assertions. From a purely scientific viewpoint, it is certainly better to work with the isolated toxin than the whole pollen grain or an extract from them such as I used at first, before I realized that the toxicity was an attribute of the albumin alone.

"Dr. O. Kammann, who investigated this matter at my request,[4] was able to prove that the albumin fraction contains the toxin and that the globulin fraction is entirely inactive.

"Having determined that the albumin of the pollen is the specific cause of hay-fever, it was possible now to carry out my experiments along quantitative lines. It is possible to extract the albumin from the pollen by means of saline solutions of proper strength and then to precipitate it with alcohol or to obtain it by dialysis, and

[4] Kammann: Zur Kenntnis d. Roggen-Pollens u. des darin enthaltenen Heufiebergiftes. Beitrage z. Chem. Physiol. u. Pathol., 1904, Bd. V, Heft. 7-8, S. 346.

then dry it. In this condition it retains its activity for many years.

"The experiments which I had done up to this time on hay-fever patients had not conformed to the natural process. In order to conform to these more closely I performed the following experiment: A hay-fever patient and a normal individual took their places in a large glass cabinet in which rye pollen had been distributed. The hay-fever patient took sick, the other remained well. It was not determined by this experiment how much of the pollen had been taken up by the hay-fever patient. The question as to whether or not enough pollen was present in the air during the hay-fever season to cause the symptoms had not been satisfactorily settled. Blackley (*vide supra*) had already made attempts to settle this question by means of a method worked out by Phœbus. He had carefully counted at different periods of the years the pollen which gathered on glass plates, whose surface had been covered with glycerin. My coworkers, especially Liefmann,[5] found that in the heart of Hamburg, while hay-fever was at its height, 250 pollen grains accumulated on a surface of one square centimeter during twenty-four hours, *i.e.*, 25,000 to the square meter. It was established that with the first appearance of the pollen in the air the patient

[5] Liefmann: Ein Beitrag zur Frage nach d. aetiologischen Bedeutung gewisser Pflanken' pollenkoerner fuer d. Heufieber. Zeitschr. f. Hyg. u. Infectionskrankheiten, 1904, Bd. 47, p. 153.

began to complain of an itching at the inner canthus of the eye; his suffering became more intense in direct proportion to the quantity of pollen in the air. On rainy days no pollen accumulated on the glass plates, altho they were protected from the rain. Early in June the pollen of the grasses far exceeded those of other plants in numbers, and from about the third week in July grew gradually less, so that at the end of July, or the beginning of August, only a few stray grains were found. Thus can be explained the periodicity of the course of hay-fever and also the occurrence of sporadic cases after the hay-fever season is over. There was still no certain method of predicting quantitatively the action of the pollen. Dr. O. Kammann had shown that the organic portion of the pollen of the grasses is about 40 per cent. albumin. He had shown further that about 20,000,000 rye pollen weighed one gram. By means of these figures we could compute the amount of toxin in a single pollen. By means of a solution of known strength of the poisonous albumin of the pollen, it could be determined how many pollen grains were necessary in any given case to produce mild, moderately severe, or severe symptoms. It was evident that different patients were susceptible in varying degrees. A concentrated solution introduced into the conjunctiva or nose of a normal individual causes no symptoms. The majority of hay-fever patients were stimulated by one drop (1-20 to 1-30 cm.) of a solution of 1 to 20,000 or 1 to 30,000.

There were patients, however, who responded to one drop of a solution diluted a million times, the equivalent of the amount of albumin contained in one to three pollen grains.

"Liefmann constructed an aeroscope by means of which he was able to determine how much pollen was taken in with each breath. In the neighborhood of a field of rye one inhales with each breath two or three pollen grains; in the middle of a large city he found that in every cubic meter of air there were about three hundred and eight.

"Thus in this way questions as to the quantitative relationship of the pollen to the attack were satisfactorily answered. By means of these experiments it had been plainly shown that the albumin of the pollen of certain plants, especially that of all grasses, is to be looked upon as the active cause of hay-fever. With my coworkers I examined the pollen of 106 plants, and found them all without any action, altho I had examined such pollen which had been considered capable of producing hay-fever. In addition to the pollen, I had been informed that in China at the time of the blossoming of Ligustrum vulgare a disease very much like hay-fever was prevalent. I examined the pollen of this plant and found it active. In Southwest Africa, when the grasses blossom, conditions like hay-fever prevail, especially among the half-breeds. One European had to forsake Africa at this time on account of his intense suffering. In Europe he remained perfectly

well. On examination it was found that he did not react to the grass pollen. In Africa, however, at this time, the acacia blossoms and it has been looked upon as the cause of the condition. This patient was unaffected by the pollen of two different species of acacia. I am in hopes that experiments which we have since then set on foot will explain this disease to us. In addition to the thirty varieties of graminaceæ and cyperaceæ, I have found the pollen of the following plants active: swamp-pink (*Lonicera caprifolium*), lily-of-the-valley (*Convallaria majalis*), hairy Solomon's seal (*Polygonatum multiforum*), Œnothera biennis, rape (*Brassica napus*), and spinach (*Spinacia oleracea*).

"Of special importance is the autumnal catarrh, which occurs in the United States of America, beginning early in September and lasting about six weeks. This autumnal catarrh is much more common in the United States than the vernal catarrh. I have had the opportunity of examining a large number of American hay-fever patients, and was able to establish the fact that those patients who only suffer in the fall do not react at all to the albumin of the grass pollen. They do react, however, regularly to the albumin of the pollen of goldenrod (*Solidago*) and of ragwood (*Ambrosia*). I have examined a large number of species of both these plants and they were all active. These patients also react to the pollen of the chrysanthemum and the other asters. Those American patients who suffer only from spring catarrh,

not from the autumnal type, react only to the grass pollen, not to that of the goldenrod or the ragweed. A third group of patients suffer from about the middle of May until early in November with a hay-fever-like affection. These unfortunates react both to the grass pollen and to the active agent of the autumnal catarrh. Goldenrod and ragweed are very widespread in the United States. They are found not only on meadows, fields, roads and along edges of woods, but grow in the midst of cities in neglected places. In Europe they do not occur naturally, indeed the goldenrod can with difficulty be made to blossom there. The pollen of goldenrod, however, is not scattered as easily as that of the ragweed. All attempts to grow ragweed in this country failed until 1911. In this year, which was extremely hot and dry, I succeeded for the first time. These facts serve as further important supports for the pollen theory. There were, however, still many questions to be settled before all this mysterious phenomena which characterize hay-fever could be explained.

"One very important question, that of individual predisposition, I have only lightly touched upon. It is clear that all people, including the inhabitants of large cities, are at certain times of the year exposed to the pollen of many plants, which settle on their skin, conjunctiva, are inhaled into the nose, and taken up into the mouth. By far the largest part of these individuals are unaffected by the pollen,


GOLDENROD, ROUGH STEMMED


SEASIDE GOLDENROD

only a very small percentage take sick. The poisonous albumin of the pollen is a substance, therefore, which is innocuous to most people, and is only active in those cases in which there is a special susceptibility. In other words, hay-fever requires an individual predisposition. This personal predisposition is present for the well-known poisons of the pharmacopœia, either not at all or at most in very slight degree. In the case of the infectious diseases it is much more evident. If, for instance, the cholera or typhoid bacillus is spread through a city by means of the water supply, only a small percentage of the inhabitants are unaffected. This can be explained on the theory that the cholera organism does not find in most individuals those conditions which are necessary to its existence and growth. The fact that only about half of the cholera patients die can be explained by similar quantitative differences. I do not know of another instance of a substance absolutely inactive as far as a part of the population is concerned, but a very virulent poison for others. The individual predisposition in a case of hay-fever must be of a peculiar sort. It might be explained that the hay-fever poison enters the circulation of some people (hay-fever patients) and not of others. That this is the case I could prove by the demonstration of antibodies in the blood of the hay-fever patients. I shall return to this subject later. Here it is sufficient to say that these specific substances could be found only at the close of the hay-fever period; six

months later they had disappeared. In normal individuals they could at no time be demonstrated. The gradual disappearance of the immune bodies is easily explained. We know from animal experiment that these substances appear a certain time after infection, gradually to disappear again. At first blush the demonstration of immune bodies in the blood of hay-fever patients would seem to be a sufficient explanation of the hay-fever predisposition. Close study makes this seem uncertain.

On continuing the experiments I found that these immune bodies were not present in all patients, indeed, in the same patient I could not find them in some cases two years in succession. The following objection to this explanation was even stronger: A colleague of mine, disposed to hay-fever, who had helped me for many years, allowed himself to be injected with a solution of pollen albumin. One half-hour after the injection marked symptoms appeared in the eyes, nose, and mouth. The patient experienced pains in the chest, expectorated a tenacious, mucoid sputum, and perspired freely. The respiration became rapid and difficult, the pulse-rate was accelerated, and the voice grew weak. After fifty minutes there was a flat, urticarial eruption over the whole body. After twenty-four hours all the results of the injection had not yet disappeared. At the site of the injection there was a marked swelling, which persisted for five days.

"Injection of hay-fever toxin caused the same

symptoms in me. A colleague who did not suffer with hay-fever reacted to the same dose with a small, almost imperceptible swelling at the site of the injection. Pollen albumin was, in other words, not toxic for him when introduced under the skin. Hundreds of experiments have proved to us that pollen albumin is not a poison in the ordinary sense of the word, and that even when introduced into the circulation it is inactive. Not only is the skin of hay-fever patients permeable, for the hay-fever poison in varying degrees, but it also reacts to the toxin in different ways in different patients. In some cases when a solution of pollen albumin is placed on the skin, there occurs within a few minutes an erythema. If, on the other hand, a patient is very susceptible to hay-fever, the skin may show absolutely no reaction when brought in contact with the toxin. These results may be of value in the study of individual predisposition, since they enable us to throw some light upon the question as to whether or not hay-fever is to be looked upon as a result of hypersensitiveness.

"In the first place, statistics have definitely proved that hay-fever has no relation to any constitutional disease,—for instance, gout; that, indeed, only a very small percentage of hay-fever patients are gouty. It is very commonly believed that hay-fever is due to some anomaly or stopping up of the upper air-passages. A local disease of the trigeminus is assumed by some, with a resulting sensitiveness on the part of certain mucous membranes. The falsity of these

conceptions is clear from the experiments cited above. Not only does the whole skin surface of many patients react to the poison, but subcutaneous infection is followed by characteristic effects. By showing that the anal mucous membrane of hay-fever patients reacts to the pollen toxin, I believe that all those hypotheses, which assume only a local sensitiveness on the part of the cranial nerves, or the capital mucous membrane, is robbed of support. Suggestion, as we have seen, plays a large part in the attempts to explain hay-fever predisposition. I can treat this question together with that of the rôle of specific odors of flowers, cats, dogs, etc. Two colorless odorless solutions were prepared, and a drop from one of them was placed on the mucous membrane of the eye and nose of a large number of hay-fever patients. Some reacted, others did not. None of them knew what sort of a solution was being used. The applications were then made in a different way, each patient receiving a drop of the solution which had not been used in his case before. Those who had reacted the first time did not do so the second. The one solution was physiologic salt, the other pollen albumin. None of the patients reacted to the saline, all reacted to the other solution. In the course of many years I repeated these experiments with many variations. In the place of the salt solution I used solution of albumin from inactive pollen. The results were always the same. In the face of such results, he who would *explain* hay-fever on the ground of suggestion,

simply ignores all the facts to the contrary, and his opinion does not deserve serious consideration.

"Hay-fever is looked upon as a result of an advanced culture and civilization. It happens that there are very few hay-fever patients in the laboring class, and that the Anglo-Saxon races, especially the Germans, English, and Americans, furnish the largest number of such patients. That hay-fever does at times occur among the Romans and other nations, I am able to gather from correspondence that I have had with inhabitants of such countries. In St. Louis I met an elevator boy who had hay-fever. Among the Anglo-Saxons the disease is found most often among professional men. Men appear to be twice as susceptible as women. It is often claimed that hay-fever follows a period of strenuous mental work, or of excitement, as, for instance, after examination, or in officers after maneuvers. Hay-fever has often been shown to be hereditary. Most frequently, however, a severe attack of influenza has left hay-fever in its wake. Other causes, as, for instance, a difficult labor, are asserted by patients to have been the exciting cause of their hay-fever attacks. May we conclude from all these facts that hay-fever is the result of a disturbance of the central nervous system?

"It was formerly believed that all hay-fever patients were very nervous and excitable. This is certainly not universally true. If we are indeed dealing with a severe abnormality of the

central nervous system this, in most instances, makes itself felt only in a hay-fever predisposition. Hundreds of hay-fever patients have written me that except during the season they are altogether well, and I have found among hay-fever patients many with phlegmatic dispositions. Those idiosyncrasies which resemble hay-fever in a way, as, for instance, susceptibility to strawberries, crawfish, iodin, antipyrin, bromids and the salts of quinin, are to-day explained on the ground of anaphylaxis.

"Th. Albrecht declares that ten years ago every physician had his own theory concerning the treatment of hay-fever. And I may add from my own experience that every patient also had his own method of treatment, which was, as a rule, very complicated. From my records it is very evident that many patients had ten or more hay-fever remedies, which they used either separately or together. A hay-fever patient takes up at once every new remedy that appears and enthusiastically recommends it to others. As a rule, he learns of the new remedy near the end of the hay-fever season, and while he is using it his troubles disappear and he attributes his relief to the remedy he has been using. In the following spring he is undeceived. In this way one hay-fever remedy after another is consigned to oblivion only to reappear later under a different name. The only remedies that have survived for any length of time are those with narcotic effects, as cocain, adrenalin, anesthesin, morphin, etc. Concerning the danger connected with the

use of these narcotics, it is surely not necessary to say a word. In addition, adrenalin and anesthesin and the remedies prepared from them cause in many cases a sensation that is much more annoying and unpleasant than hay-fever itself. I, myself, have tested all the hay-fever remedies on which I could lay my hands within the last ten years. With no one of them did I accomplish a beneficial result. There was indeed no reason to suppose that the remedy could accomplish the things that were claimed for it. It is easy to gather the same opinion if one reads the thousands or more hay-fever histories that I have in my possession. I have called attention above to the fact that on purely theoretical grounds nothing was to be expected from these preparations, and that chance had not put into our hands a chemical preparation that was effective. Every physician must warn his patients against the use of narcotics. I shall, therefore, not consider these remedies and methods of treatment that belong to this category.

"In the thousands or more histories which I have been able to read, cauterization, burning, chiseling, and sawing in the nose play a large part.

"It has been shown that the active albumin pollen is a substance of such marked specificity that the albumin which causes hay-fever symptoms in one patient (pollen of the grasses in Europeans) is entirely inactive in other patients (those with autumnal catarrh). On the other hand, the toxin of the ragweed has absolutely

no effect on the European patients. By means of the complement deviation method I could prove that this specificity could be shown in the hemolytic properties of the different albumins, the albumin of the grass pollen reacting altogether differently from that of goldenrod and ragweed. In view of this state of affairs, it is not to be hoped that chance would furnish us a chemical substance that would either neutralize or render inactive the pollen albumin, or overcome the individual predisposition, which, as we have seen, is also strictly specific. I have come to the conclusion that we can accomplish our end in three ways only.

"First, by finding localities where the specific cause does not occur; second, by protecting the eyes, nose and mouth of the patient from the pollen; third, by active immunization against the toxin, or the use of a specific antitoxin.

"The first method is yearly employed by many patients with success. The second method is also successful. Hay-fever patients are free from symptoms in regions in which a specific pollen does not occur. This was to be expected from what we have learned about the cause of the disease. Thus many patients find relief on the seashore, in islands, and in barren mountainous districts. In Germany they go to Heligoland. In the United States they retire to Fire Island, Long Beach, the White Mountains, Green Mountains, or Adirondack Mountains during the hay-fever season.

"All my attempts of many years to get rid

of the irritating contents of the horse serum have been in vain. As early as 1905, I realized that this would be so, for I proved then that the irritating substance (as I then called the anaphylactic agent) was bound to the euglobulin of the horse serum as was also the antitoxin itself. If the euglobulin is destroyed the antitoxin is at the same time rendered useless. I have been able to help patients who have become anaphylactic in two ways: First, by the use of pollantin R., and the suggestion to use this diluted serum only before the occurrence of the hay-fever attack, in the very smallest doses, and if possible only once daily. Patients who followed these directions have informed me that pollantin R. did not irritate them at first, altho it did so later. The irritation was, however, not severe and disappeared within ten to thirty minutes. After this the patient was free from hay-fever attacks for one or more days. Secondly, I have taken advantage of the fact that horse serum anaphylaxis is in most cases specific, but does not appear to me to be always so. I have seen instances in which during the development of a hypersensitiveness to one animal serum, patients were rendered anaphylactic to the sera of other animals also. This does not, however, happen often. I have, therefore, administered to patients who could no longer stand pollantin R., a very active rabbit serum with good results. It was not only possible to ward off attacks with this serum, but also to protect patients from further attacks during the hay-fever season.

These results appear to me to support the opinion, which I exprest years ago, viz., that the reaction to the antitoxin, and with it the tendency toward definite immunization, is directly proportional to the degree to which anaphylaxis toward animal serum develops. Patients who have become anaphylactic get along with much smaller doses of antitoxin than other patients, and have, I believe, a better chance to effectually overcome their hay-fever predisposition.

"This is the goal toward which we must strive. I know of many hay-fever patients, some of whom had attacks of the worst kind, who were entirely free after the use of pollantin for a very short time. I consider these people permanently cured, and so exprest myself in an article last year. A rhinologist interested in hay-fever wrote to me that he could not understand these successes, and that he and his colleague had never been able to obtain such results. He wrote further that my successful experiences were in marked contrast to the experienced German Hay-Fever Association. In answer to such communications I have placed my material in the hands of the secretary of this Association, Dr. Th. Albrecht. I was very much pleased to learn as a result that Dr. Albrecht had been able to cure and successfully immunize patients by means of pollantin. In a recent publication, Dr. Albrecht reported twelve cases in which, after the use of pollantin for a short time, there resulted either a complete cure or at least a marked improvement. These observa-

tions are, of course, of intense interest to me. I would ask all colleagues who have made similar observations to be kind enough to communicate them to me. I have only been strengthened in my former opinion that by means of a mixed passive and active immunization a permanent cure of hay-fever can be accomplished.''

6. Frequent Causes and the Treatment of Seasonal Hay-Fever*

By Chandler Walker, M.D.

BOSTON

Although John Bostock,[1] in 1819, first described the symptom complex of hay-fever, it was not until 1873 that Blackley[2] determined the real cause of the symptoms, namely, the pollen of plants. Curtis,[3] in 1900, was the first to attempt to produce active immunity or to treat the condition; he used extracts of the whole plant. Since Dunbar,[4] in 1905, was the first to

* From the medical clinic of the Peter Bent Brigham Hospital. Reprinted from the ''Archives of Internal Medicine,'' July, 1921, Vol. XXVIII, pp. 71-118. Copyright, 1921, American Medical Association, Chicago.

[1] Bostock, J.: Case of Periodical Affection of the Eyes and Chest, Med. Chir. Tr., Lond. 10:161, 1819.

[2] Blackley, C. H.: Experimental Researches on the Causes and Nature of Catarrhus Aestivus (Hay-Fever or Hay Asthma), London 7:202, 1873.

[3] Curtis, H. H.: The Immunizing Cure of Hay Fever, Med. News 77:16 (July 7), 1900.

employ extracts of the plant pollen, the modern treatment of hay-fever was really begun by him. During the past ten years reports on the treatment of hay-fever have been too numerous to justify reference to all of them in this paper, but the work of Noon, Freeman, Koessler, Cooke, Scheppegrell, Goodale, Selfridge and possibly of others justify the mention of their names since it is these who have done most toward establishing the treatment of seasonal hay-fever.

Notwithstanding the number of papers on the subject, there is a paucity of specificity as regards the pollens that actually cause hay-fever, and, likewise, the treatment of the condition has been stated too often in a general way. As a result, there would seem to be as many different pollens actually causing hay-fever and as many different ways of treating hay-fever as there have been investigators. A natural result was that commercial houses have put on the market pollen preparations consisting of mixtures of the various pollens that prevailed at definite seasons, and these mixtures were used by the medical profession all over the country. In other words, neither the physician nor the commercial house have been concerned as to whether any particular pollen was indigenous and caused hay-fever in one locality to the exclusion of other pollens in other localities, and the physician would not or could not determine by tests which of the prevail-

[4] Dunbar, W. P.: Berl. klin. Wchnschr. 17:797, 877, 915, 942, 1237, 1905; Deutsch. med. Wchnschr. 32:578, 1911.

ing pollens was the actual cause of symptoms; the pollen mixtures were used hit or miss. From the practical standpoint, the results from such treatment could not be as satisfactory as would be the case if the patient were treated by the pollens to which he was actually exposed and to which he was most sensitive. Therefore, the excuse for publishing the present paper in considerable detail is to help clarify the present status of the treatment of seasonal hay-fever as regards patients living in the New England States, and it hoped that other investigators in the same and in other localities will be stimulated to detail their investigations. It is only by such detailed reports that it will be possible to learn the prevailing causative pollens in various localities and the best method of treatment.

After a description of the methods used by me in testing and treating hay-fever patients, this paper will consist of a series of tables. Table 1 presents those patients who were treated with ragweed pollen only one year; Table 2, patients treated with grass pollen only one year; Table 3, patients who had insufficient treatment with ragweed and with grass pollen; Table 4, patients treated two years in succession with ragweed pollen; Table 5, patients treated two years in succession with grass pollen; Table 6, patients treated three successive years with ragweed pollen; Table 7, those treated three successive years with grass pollen, and Table 8, those treated four successive years with ragweed pollen. In all of these tables the patients were

treated preseasonally, thereby attempting to prevent symptoms. Table 9 presents patients who were treated during the season with grass pollen; Table 10, those treated during the season with ragweed pollen, and Table 11, patients treated during the season with bacterial vaccines. In these tables the patients were treated during the season, thereby attempting to relieve symptoms. Table 12 presents patients treated both preceding and during the season. The pollens of trees and pollens other than those already mentioned will be discust as possible causes of hay-fever. Finally, other parts of plants, animal emanations, foods, bacteria and olfactory irritants will be discust as causes of seasonal hay-fever.

The cutaneous or skin test, which has proven satisfactory to me,[5] was employed to determine the sensitivity of the patients to the various pollens. A number of small cuts, each about an eighth of an inch long, are made on the flexor surfaces of the forearm. These cuts are made with a sharp scalpel, but are not deep enough to draw blood, altho they do penetrate the skin. On each cut is placed a pollen and to it is added a drop of tenth normal sodium hydroxid solution to dissolve the pollen protein and to permit of its rapid absorption. Instead of using the whole pollen, a concentrated solution of pollen protein or extract may be used without

[5] Walker, I. C., and Adkinson, J.: A Comparison Between the Cutaneous and the Intradermal Tests in the Sensitization of Asthmatic and Hay Fever Patients, J. M. Research 37:287, 1917.

the addition of sodium hydroxid. At the end of half an hour the pollens are washed off and the reactions are noted, always comparing the inoculated cuts with normal controls on which no pollen was placed. A positive reaction consists of a raised white elevation or urticarial wheal surrounding the cut. The smallest reaction that we consider positive must measure 0.5 cm. in diameter. All larger reactions are noted by a series of plus marks; any smaller reaction is called doubtful. The method of obtaining pollen from the flower has been outlined in Study 11.[6]

Having determined by these tests which pollens give a positive reaction, before a patient can be treated with the pollen it is necessary to know how sensitive that patient is to the pollen; therefore, different strengths of solutions of the pollen protein are tested in a similar manner. These solutions are made as follows: To 0.5 gm. of the dry pollen is added 44 c.c. of sterile physiologic sodium chlorid solution, and the mixture is shaken thoroughly at frequent intervals for twenty-four hours, after which enough absolute alcohol (6 c.c.) is added to the mixture to make the alcoholic content 12 per cent. Again, the mixture is thoroughly shaken at frequent intervals for twenty-four hours, after which it is centrifugalized at high speed and the supernatant fluid is pipetted off and saved. This supernatant fluid, therefore, consists of the pollen

[6] Walker, I. C.: Studies on the Sensitization of Patients with Bronchial Asthma to the Various Pollens, J. M. Research 36:237, 1917.

protein dissolved in a 12 per cent. alcoholic physiologic sodium chlorid solution and it represents, by weight, 1 part pollen to 100 parts solvent. This 1:100 solution is used as stock, and from it other dilutions, 1 500, 1:1,000, 1:5,000 and 1:10,000 are made, using a 12 per cent. alcoholic physiologic sodium chlorid solution as a diluent. These solutions are used not only for the skin tests but for treatment, and with the addition of a small crystal of thymol they keep for many months in a cool place.

Method of Treating Preseasonally with the Pollen Extracts Follows.—The first treatment consists of from 0.1 to 0.2 c.c. of that dilution next higher than the one which gave a positive skin test, or, in other words, the first dose is 0.1 c.c. or 0.2 c.c. of the strongest dilution which failed to give any skin reaction whatever, no matter how slight. With our pollen extracts the majority of patients whom we treated gave a more or less positive reaction with the 1:5,000 dilution, therefore, the first treatment consisted of 0.1 c.c. or 0.2 c.c. of the 1:10,000 dilution. Treatments were given subcutaneously once a week, and each week the amount of the extract was gradually increased, so that as the treatment progressed, stronger and stronger dilutions were used, until one or more doses of the 1:100 dilution were given. As an example, I will give what I have found by experimentation to be the best outline of treatment for a patient who gives a more or less positive skin test with a 1:5,000 dilution of pollen extract; 1:10,000, give 0.15

c.c.; 1:5,000, give 0.15 c.c., 0.25 c.c., 0.35 c.c., 0.45 c.c.; 1:1,000, give 0.15 c.c., 0.25 c.c.; 1:500, give 0.15 c.c., 0.25 c.c., 0.35 c.c., 0.45 c.c.; 1:100, give 0.15 c.c., 0.2 c.c., 0.25 c.c. Each dose was given preferably at weekly intervals and never oftener than once every five days

This schedule of treatment calls for fourteen inoculations; however, for some reason or other, modifications frequently have to be used. An occasional patient is so sensitive to the pollen that a 1:10,000 dilution gives a slight reaction, thus necessitating an initial dose of 0.15 c.c. of 1:20,000 followed by possibly two doses of 1:10,000. Often it happens that a patient has considerable local or general reaction following some one treatment in the schedule, thus necessitating the repetition of that particular dose before the next increase may be given. More often the patient presents himself for treatment too late to complete the scheduled series of treatments before the onset of pollination so that for preseasonal treatment alone, some of the final treatments in the schedule must be omitted. This schedule is often modified purposely with certain individual cases. For instance, in some cases the second treatment with the 1:1,000 dilution, namely, 0.25 c.c., is omitted, and in some cases instead of giving 0.15 c.c. of the 1:100 dilution, when this happens to be the final treatment that the patient is to receive because of onset of pollination, a fifth treatment with the 1:500 dilution, namely, 0.55 c.c., is often substituted, and even a sixth treatment with the 1:500 dilution,

namely, 0.65 c.c., is sometimes given. These larger doses of 1:500 approximate the amount of protein in 0.15 and 0.2 c.c. of the 1:100 dilution, therefore, the fifth and sixth treatment with the 1:500 dilution, as outlined, is practically the equivalent of giving 0.15 c.c. and 0.2 c.c. of the 1:100 dilution. Since by far the great majority of patients are treated from three to five times with the 1:500 dilution, and since this number of treatments has given fairly satisfactory results, I consider this number of treatments, which consists usually of a total of ten, as worth giving, although a continuance of the schedule beyond three doses of the 1:500 dilution is most desirable, and giving less than three treatments with the 1:500 dilution is undesirable. Tables 1 and 2 will illustrate the results obtained from giving three or more treatments with the 1:500 dilution, and Table 3 will illustrate the results obtained from giving less than three treatments with the 1:500 dilution.

Since in the New England States the majority of patients have the first hay-fever symptoms between Aug. 10 and 20, during which time the compositae, chiefly ragweed, begin to pollinate, in order to complete the above schedule just previous to the onset of symptoms and pollination, patients must begin treatment between the last week in April and the first two weeks in May. Beginning treatment the first week in June will permit of giving from three to five treatments with the 1:500 dilution. Likewise, since the early type of hay-fever, or so-called rose cold,

which is usually caused by the grasses, begins the last few days of May or the first of June, treatment for this type of hay-fever should begin about the first of March, and the starting of treatment as late as the first of April will not permit of more than three or four treatments with the 1:500 dilution, according to the schedule outlined. Naturally, in localities outside of New England, these seasons would differ, and the beginning of treatment consequently would vary, also the causative pollen must differ.

Before Table 1 may be discust, attention should be called to the following facts: In the New England States ragweed (*ambrosia artemisifolia,* or dwarf ragweed) is not the only plant that pollinates during August and September, nor is it the only pollen to which individuals are exposed or with which patients were tested. Most of the compositae, such as goldenrod, sunflower, golden-glow and aster, pollinate during August and September; daisy pollinates during June and July, and dandelion in the early spring; giant ragweed is rarely encountered in the New England States. In order to simplify the table, and because in my experience pollens other than ragweed rarely, if ever, are the chief cause of symptoms during the late hay-fever season, only ragweed is mentioned in the table although tests were made with the other pollens. During the years 1917, 1918, and 1919 all of the patients in Table 1 were with goldenrod and daisy, and the majority were tested with golden-glow and sunflower. During 1920 many

of the patients were tested with these pollens. One hundred and twenty patients in Table 1 were tested with the pollens of daisy and golden-rod, and 100 were also tested with the pollen of sunflower and golden-glow. Fifty per cent. of those tested with golden-glow and with sunflower gave a positive reaction with the whole pollen, but none of these gave a reaction with a 1:100 dilution of the pollen; the other 50 per cent. failed to react with the whole pollen. Therefore, it may safely be stated that the pollens of golden-glow and sunflower are not primarily causes of hay-fever in New England. Of those tested with daisy pollen, 65.5 per cent. failed to react to a 1:100 dilution of daisy pollen; 21 per cent. did react to the whole pollen but not to a 1:500 dilution; 10 per cent. reacted more or less positively to a 1:500 dilution of the pollen, and only 3.5 per cent. reacted to as high a dilution as 1:1,000. Therefore, in comparison with ragweed, in only 3.5 per cent. could one consider that daisy might be a cause of hay-fever as judged by tests, but it should be borne in mind that daisy pollinates during June and July and has finished pollination before ragweed begins, therefore daisy cannot complicate the causes of August and September hay-fever. Of the 120 patients in Table 1 who were tested with golden-rod pollen, 78.5 per cent. failed to react with a 1:100 dilution of the pollen; 10 per cent. did not react to a 1:500 dilution of the pollen; 8.25 per cent. did react more or less to a 1:500 dilution, and 3.25 per cent. reacted to a 1:1,000 dilution

TABLE 1.—PRESEASONAL TESTS AND TREATMENT WITH RAGWEED POLLFN

G = Good. F = Fair. N = None.

Patient	Age of Onset	Duration	Tests Before Treatment	Number Treatments with Final Dilution	Tests at End of Treatment	Result of Treatment*
			Season 1917			
1	42	25	1-1,000±	1-100:4	....	G.
2	8	7	1-5,000±	1-100:2	1-100+	G.
3	44	30	1-1,000+	1-100:2	1-100+	G.
4	18	10	1-5,000±	1-500:5	....	G.
5	17	21	1-5,000±	1-100:2	1-500±	G.
6	26	4	1-5,000±	1-500:4	1-500+	G.
7	24	16	1-5,000±	1-100:3	1-500+	75%
8	43	5	1-5,000±	1-500:3	....	50%
9	30	8	1-5,000+	1-500:6	....	G.
10	43	3	1-10,000+	1-500:4	....	G.
11	10	23	1-5,000±	1-100:4	....	G.
12	1	11	1-1,000±	1-500:3	....	50%
			Season 1918			
13	21	12	1-10,000±	1-500:4	....	50%
14	8	5	1-1,000±	1-100:2	....	N.
15	..	..	1-1,000±	1-500:5	....	N.
16	..	6	1-10,000±	1-500:4	....	G.
17	32	3	1-5,000±	1-100:3	....	F.
18	22	15	1-5,000±	1-500:4	....	75%
19	22	18	1-5,000±	1-500:5	....	G.
21	24	30	1-10,000+	1-500:5	....	N.
20	38	20	1-5,000±	1-100:1	....	50%
22	25	4	1-5,000+	1-100:2	....	G.
23	24	4	1-5,000±	1-500:6	....	75%
24	33	25	1-10,000±	1-500:5	....	N.
25	26	20	1-1,000±	1-100:1	....	F.
26	1	35	1-5,000±	1-500:3	....	75%
27	28	14	1-1,000±	1-500:4	....	G.
28	28	26	1-5,000±	1-500:5	....	G.
29	24	37	1-1,000±	1-500:4	....	75%
30	39	17	1-5,000±	1-500:3	....	F.
31	27	4	1-1,000+	1-500:6	....	G.
32	7	10	1-5,000±	1-500:4	....	75%
33	27	25	1-5,000+	1-500:4	....	N.
34	18	22	1-5,000±	1-500:6	....	50%
35	19	15	1-5,000±	1-500:3	....	50%
35a	27	10	1-1,000±	1-500:4	....	F.
36	18	20	1-5,000±	1-500:4	....	G.
36a	30	5	1-1,000±	1-500:4	....	G.
37	32	13	1-10,000±	1-500:4	....	75%
38	13	37	1-1,000±	1-100:3	....	75%
39	4	10	1-5,000±	1-500:3	....	G.
40	19	4	1-5,000±	1-500:3	....	50%
41	18	19	1-5,000±	1-500:5	....	75%

* Fair in result column means practically free from symptoms; good means entirely free.

TABLE I.—PRESEASONAL TESTS AND TREATMENT WITH RAGWEED POLLEN (Continued)

G = Good. F = Fair. N = None.

Patient	Age of Onset	Duration	Tests Before Treatment	Number Treatments with Final Dilution	Tests at End of Treatment	Result of Treatment*
			Season 1919			
42	24	15	1-10,000±	1-100:5	1-100+	75%
43	39	45	1-10,000±	1-500:3	1-500±	G.
44	3	8	1-10,000±	1-100:2	1-100±	G.
45	32	8	1-10,000±	1-100:4	1-100+	50%
46	20	13	1-10,000±	1-100:5	1-500±	G.
47	1	38	1-5,000±	1-500:4	....	F.
48	1	20	1-10,000±	1-100:2	1-500+	50%
49	50	3	1-10,000±	1-500:5	....	G.
50	8	9	1-10,000±	1-100:2	1-100+	G.
51	29	31	1-10,000±	1-100:3	1-100±	G.
52	37	11	1-5,000±	1-500:5	1-100±	75%
53	7	24	1-20,000±	1-100:3	1-100+	G.
54	30	9	1-20,000+	1-100:1	1-1,000+	N.
55	37	4	1-10,000±	1-100:4	1-100+	N.
56	16	7	1-10,000±	1-500:4	....	F.
57	19	12	1-5,000+	1-100:4	1-100±	50%
58	26	6	1-1,000±	1-500:5	1-100.0	G.
59	17	19	1-5,000±	1-500:3	1-500+	50%
60	2	17	1-5,000±	1-100:4	1-500±	75%
61	28	16	1-5,000+	1-100:4	1-500+	G.
62	27	22	1-10,000±	1-500:5	....	75%
63	22	30	1-10,000+	1-500:5	....	75%
64	10	3	1-500±	1-100:2	1-100.0	G.
65	6	10	1-500+	1-100:4	....	G.
66	45	5	1-10,000±	1-100:3	1-100+	G.
67	4	10	1-10,000±	1-100:2	1-500+	G.
68	32	3	1-1,000±	1-500:4	....	G.
69	38	7	1-20,000+	1-100:2	1-1,000+	N.
70	22	6	1-1,000±	1-100:4	1-100.0	G.
71	30	4	1-10,000±	1-500:2	....	F.
72	27	7	1-10,000±	1-100:4	1-1,000±	N.
73	16	45	1-5,000±	1-500:4	....	G.
74	8	26	1-10,000+	1-500:5	1-500+	75%
75	49	20	1-5,000±	1-100.4	1-100+	G.
76	39	16	1-500+	1-100:1	....	G.
77	36	37	1-10,000±	1-100:3	1-1,000±	G.
78	17	3	1-10,000±	1-500:4	1-500±	G.
79	25	10	1-10,000±	1-500:4	....	50%
80	34	12	1-5,000+	1-100:3	1-100.0	F.
81	1	3	1-5,000+	1-500:5	....	G.
82	36	4	1-5,000	1-100:2	1-500±	F.
83	22	18	1-5,000±	1-500:5	1-5,000±	N.
84	16	4	1-10,000±	1-100:1	1-100.0	F.
85	38	6	1-10,000±	1-100:1	1-100±	F.

* Fair in result column means practically free from symptoms; good means entirely free.

TABLE I.—PRESEASONAL TESTS AND TREATMENT WITH RAGWEED POLLEN (Continued)

G = Good. F = Fair. N = None.

Patient	Age of Onset	Duration	Tests Before Treatment	Number Treatments with Final Dilution	Tests at End of Treatment	Result of Treatment*
			Season 1920			
86	14	7	1-5,000±	1-500:5	....	F.
87	20	6	1-10,000+	1-500:5	....	50%
88	44	8	1-10,000+	1-500:4	1-1,000±	50%
89	18	10	1-20,000±	1-500:5	....	50%
90	15	2	1-5,000±	1-500:5	....	75%
91	28	20	1-10,000±	1-100:2	....	G.
92	10	20	1-5,000±	1-500:4	1-100±	75%
93	8	2	1-500+	1-100:4	....	75%
94	33	12	1-5,000+	1-500:5	....	F.
95	35	35	1-20,000+	1-500:5	1-500+	75%
96	12	5	1-10,000	1-500:4	....	75%
97	9	8	1-10,000±	1-500:4	....	F.
98	37	3	1-10,000±	1-500:5	1-500±	75%
99	9	8	1-10,000±	1-100:2	....	75%
100	..	1	1-5,000±	1-500:6	....	75%
101	2	12	1-5,000±	1-500:5	....	75%
102	29	6	1-5,000±	1-500:4	....	F.
103	15	30	1-10,000±	1-500:3	....	50%
104	30	15	1-10,000±	1-500:3	....	50%
105	23	1	1-1,000±	1-500:6	....	75%
106	29	40	1-5,000±	1-500:6	....	50%
107	..	8	1-5,000+	1-100:3	....	75%
108	24	1	1-5,000±	1-500:4	....	N.
109	39	10	1-5,000±	1-500:5	....	50%
110	1	9	1-5,000±	1-500:5	....	F.
111	12	9	1-10,000±	1-500:5	....	50%
112	30	5	1-10,000±	1-500:5	....	50%
113	8	27	1-5,000±	1-500:5	....	75%
114	3	2	1-5,000±	1-500:5	....	F.
115	30	5	1-5,000+	1-500:5	....	50%
116	41	2	1-5,000±	1-500:5	....	75%
117	2	17	1-10,000±	1-100:3	....	F.
118	8	23	1-10,000±	1-500:6	....	F.
119	Infant	23	1-10,000±	1-500:4	....	75%
120	Infant	21	1-5,000±	1-500:5	....	50%
121	24	12	1-5,000±	1-500:5	....	G.
122	30	8	1-5,000+	1-500:5	....	F.
123	12	5	1-10,000±	1-500:5	....	75%
124	Infant	33	1-20,000±	1-500:4	....	50%
125	10	5	1-10,000±	1-500:3	....	75%
126	35	7	1-5,000±	1-500:4	....	75%
127	2	47	1-5,000±	1-500:5	....	F.
128	14	10	1-5,000±	1-500:5	....	F.
129	17	2	1-5,000±	1-500:4	....	50%

* Fair in result column means practically free from symptoms; good means entirely free.

TABLE I.—PRESEASONAL TESTS AND TREATMENT WITH RAGWEED POLLEN (Continued)

G = Good. F = Fair. N = None.

Patient	Age of Onset	Duration	Tests Before Treatment	Number Treatments with Final Dilution	Tests at End of Treatment	Result of Treatment*
			Season 1920	—Cont'd		
130	33	3	1-5,000±	1-500:3	....	F.
131	20	10	1-1,000±	1-500:5	....	75%
132	29	10	1-1,000±	1-500:5	....	50%
133	19	15	1-5,000+	1-500:5	....	50%
134	16	6	1-5,000±	1-500:3	....	N.
135	27	12	1-10,000±	1-500:5	1-100	50%
136	49	5	1-20,000±	1-500:4	....	75%
137	34	1	1-20,000±	1-500:3	....	50%
138	4	6	1-5,000±	1-500:4	....	F.
139	26	8	1-5,000±	1-500:4	....	75%
140	33	2	1-5,000±	1-500:3	....	75%
141	15	6	1-5,000+	1-500:5	....	50%
142	8	2	1-5,000±	1-500:4	....	75%
143	5	35	1-5,000±	1-500:5	....	75%
144	25	6	1-5,000±	1-500:5	....	N.
145	32	10	1-10,000±	1-500:5	....	F.
146	20	6	1-1,000+	1-500:4	....	F.
147	10	20	1-5,000+	1-500:4	....	75%
148	35	5	1-5,000+	1-500:5	....	F.
149	22	8	1-10,000±	1-500:4	....	75%
150	33	4	1-5,000±	1-500:5	....	50%
151	16	4	1-5,000±	1-500:3	....	75%
152	24	2	1-5,000±	1-500:4	....	50%
153	9	45	1-10,000±	1-500:5	....	G.
154	20	2	1-5,000+	1-500:4	....	75%
155	24	6	1-5,000±	1-500:5	....	50%
156	21	20	1-5,000±	1-500:5	....	75%
157	30	25	1-5,000±	1-500:5	....	F.
158	4	3	1-500+	1-500:6	....	50%
159	10	20	1-10,000±	1-500:4	....	50%
160	18	4	1-5,000±	1-100:1	....	75%
161	17	3	1-10,000±	1-500:4	....	75%
162	29	5	1-10,000±	1-500:4	....	F.
163	36	2	1-20,000±	1-500:5	1-1,000±	F.
164	7	5	1-1,000+	1-500:5	....	75%
165	19	1	1-500±	1-500:4	....	75%
166	..	25	1-20,000±	1-500:5	....	75%
167	30	5	1-5,000±	1-500:5	....	75%
168	5	4	1-5,000±	1-100:1	Pol. 0	50%
169	15	3	1-10,000+	1-100:2	....	75%
170	27	1	1-1,000±	1-500:3	....	50%
171	29	8	1-10,000+	1-500:3	....	50%
172	10	54	1-10,000+	1-100:1	....	G.
173	14	10	1-10,000+	1-500:4	....	75%

* Fair in result column means practically free from symptoms; good means entirely free.

TABLE I.—PRESEASONAL TESTS AND TREATMENT WITH RAGWEED POLLEN (Continued)

G = Good. F = Fair. N = None.

Patient	Age of Onset	Duration	Tests Before Treatment	Number Treatments with Final Dilution	Tests at End of Treatment	Result of Treatment*
			Season 1920	—Cont'd		
174	26	2	1-10,000±	1-100:2	....	75%
175	19	2	1-5,000±	1-500:5	....	G.
176	18	7	1-5,000±	1-500:5	....	F.
177	8	5	1-10,000±	1-500:4	1-1,000±	75%
178	33	2	1-1,000±	1-100:2	1-5,000±	50%
179	29	5	1-5,000+	1-100:3	....	75%
180	8	20	1-1,000+	1-100:3	1-100+	F.
181	3	9	1-10,000±	1-500:3	....	50%
182	26	10	1-5,000±	1-100:1	1-500±	75%
183	30	7	1-10,000±	1-100:2	1-500±	75%
184	10	8	1-40,000±	1-500:4	1-1,000+	50%
185	28	10	1-10,000±	1-500:5	....	50%
186	35	15	1-10,000±	1-500:5	1-500±	75%
187	11	28	1-10,000±	1-500:4	....	50%
188	1	28	1-5,000+	1-100:4	1-100+	G.
189	16	6	1-20,000±	1-500:4	....	50%
190	20	10	1-1,000±	1-100:2	....	F.
191	6	13	1-10,000±	1-500:5	....	75%
192	30	10	1-5,000±	1-500:5	....	75%
193	13	4	1-5,000±	1-500:5	....	50%
194	25	5	1-5,000+	1-500:6	....	F.
195	4	5	1-5,000±	1-100:3	....	50%
196	..	5	1-5,000±	1-500:5	....	F.
197	8	14	1-10,000±	1-500:6	....	50%
198	27	20	1-10,000+	1-500:6	....	75%
199	15	25	1-10,000±	1-500:6	....	75%
200	28	20	1-5,000±	1-500:5	....	F.

* Fair in result column means practically free from symptoms; good means entirely free.

but no higher. Therefore, in comparison with ragweed, in only 3.25 per cent. of the cases in Table 1 could goldenrod pollen be assumed as a possible cause of hay-fever. From the investigations of Scheppegrell[7] and others we know that the pollens of goldenrod, sunflower, golden-glow,

[7] Scheppegrell, W.: Hay-Fever and Hay-Fever Pollens, Arch. Int. Med. 19:959 (July), 1917.

daisy and aster are not carried by the wind, and that their pollens are heavy and shed very sparingly, so that for these reasons patients are not exposed to these pollens unless the flowers are kept in the house or unless sensitive patients smell of the flowers; naturally, the patient can refrain from such intimate contact and need not be treated for these.

Since the construction of Table 1 may not be entirely clear, the case of the second patient will be discust in detail as an example of all of the remaining cases presented in this and similar tables. Patient 2 began to have hay-fever at the age of 8; he had it for seven years; previous to treatment his skin test with ragweed pollen was slightly positive with a 1:5,000 dilution, therefore, treatment was begun with 0.15 c.c. of 1:10,000 dilution. The schedule of treatments was carried out until he was given two treatments with the 1:100 dilution; at the end of treatment his skin test was positive with the 1:100 dilution, but it should be assumed that the test was negative with weaker dilutions, namely, 1:500, etc.; the result was that the patient was free from hay-fever during the August and September season in 1917. Other symbols that may need explanation are the following: In the result column "good" means entirely free from symptoms, "fair" means practically free, that is, not entirely free from symptoms but much better than 75 per cent.; "75 per cent." and "50 per cent." mean that amount of freedom or benefit; "none" means no benefit or no relief; however,

some of these patients did claim to be 25 per cent. relieved, but I do not wish to tabulate so little benefit.

The results of treatment from the symptomatic standpoint in the 202 patients presented in Table 1 were as follows: 45 patients, or 22 + per cent., had no symptoms; 36 patients, or 17 + per cent., were practically free from symptoms; 61 patients, or 30 + per cent., were benefited at least 75 per cent.; 47 patients, or 23 + per cent., were benefited only 50 per cent., and 13 patients, or 6.5 per cent., were not benefited at all. Correlation of symptomatic benefit with the amount of treatment brings out the following facts: Of the forty-five patients who were entirely free from symptoms, twenty-three were given one or more treatments with the 1:100 dilution and twenty others were given four or more treatments with the 1:500 dilution. Of the thirty-six patients who were practically free from symptoms, one-fourth received the 1:100 dilution from one to three times, practically one-half of the series were given the 1:500 dilution five or six times, and nearly one-fourth were treated four times with this dilution. Of the sixty-one patients who were 75 per cent. improved, practically one-fifth were treated from one to five times with the 1:100 dilution, nearly one-half were treated five or six times with the 1:500 dilution, a few more than one-third were treated four times with the 1:500 dilution. Of the forty-seven patients who were 50 per cent. relieved, only seven, or approximately one-seventh, were treated with

the 1:100 dilution, approximately three-eighths were given the 1:500 dilution five or six times, about one-fifth were given four treatments with the 1:500 dilution, and nearly one-fourth were given only three treatments with the 1:500 dilution. The thirteen patients who were not benefited will be discust in detail later. Therefore, it is very evident that one or more treatments with the 1:100 dilution yielded the best results, and that five or more treatments with the 1:100 dilution yielded the best results, and that five treatments with the 1:500 dilution gave considerable better results than four treatments with this dilution, altho four treatments with the 1:500 dilution are well worth giving; as the number of patients who were treated three times with the 1:500 dilution increased, the amount of benefit gradually decreased, until nearly one-quarter of the 50 per cent. benefited fell into this group; in other words, only three treatments with the 1:500 dilution give poor results in comparison to giving four or better still five treatments with this dilution. When one stops to consider that the fifth or sixth treatment with the 1:500 dilution is equivalent in amount of protein to at least one treatment with the 1:100 dilution, it is very evident that five or six treatments with the 1:500 dilution, or one treatment with the 1:100 dilution, is the ideal treatment.

Although little information is obtained by analyzing the table in regard to why some patients were more benefited than others, and why

some were not benefited at all, after all it does seem worth doing.

Concerning the thirteen patients who were not improved, none gave positive skin tests with the pollens of daisy, goldenrod, golden-glow or sunflower. The treatment of Patient 144 was given at irregular intervals; Patient 134 lost three weeks during treatment so that he could be given only three doses of the 1:500 dilution; Patient 108 was given only four doses of the 1:500 dilution; even tho many other patients were greatly benefited by similar treatment, it may be fair to assume that the negative result with these three particular cases was due to insufficient treatment. Patient 83 gave as positive a skin test at the end of treatment as he did before treatment, and the last treatment produced an anaphylactic shock manifested by urticaria. Patients 72, 69 and 54 gave positive skin tests with a 1:1,000 dilution at the end of treatment, in spite of the fact that they all had received the 1:100 dilution one or more times. It may be safely stated that in the case of these four patients treatment did not desensitize the skin, and it is likewise probably true that, for some unknown reason, the patient's mucous membranes were not desensitized or that there was lack of union between the patients' antibodies and the treatment antigen. Patient 55 received four doses of the 1:100 dilution and at the end of treatment no dilution stronger than the 1:100 gave a positive reaction, and Patient 14 was treated with the 1:100 dilution two times, so that

these two patients ought to have had sufficient pollen treatment. Patients 33, 24, 21, and 15 all received the 1:500 dilution five times so that they also did not fall short of the average amount of treatment. The varying ages of onset and years of duration of symptoms, and the approximately equal distribution between the two sexes and between the three different years, furnish no clues toward the cause of failure from treatment. It would seem that we must blame the individuality or idiosyncrasy of these particular patients for the time being, and, therefore, it should be admitted that with our present knowledge there are a few hay-fever victims who are not benefited by preseasonal pollen therapy.

Of the forty-seven patients who were only 50 per cent. improved, three showed evidence of lack of desensitization, as was noted in the previous paragraph, in that one case following four treatments with the 1:500 dilution and another following six similar treatments gave positive skin tests with a 1:1,000 dilution of the pollen protein; the third gave a positive skin test with the 1:5,000 dilution following two doses of 1:100, and it is interesting that this patient was not shocked. It is difficult to explain why fifteen patients who were treated five times with the 1:500 dilution, and three patients who were similarly treated six times should not receive more than 50 per cent. relief when so many more experienced greater benefit from the same treatment. It is still more difficult to understand why the six patients who were treated from

one to four times with the 1:100 dilution of pollen protein should be only 50 per cent. improved, especially since at the end of treatment one patient gave negative tests with the whole pollen protein and two others gave positive reactions with no stronger than the 1:100 dilution.

Attention should be called to the decreased sensitivity of the patient as evidenced by the skin test following a satisfactory series of treatments. Fifty-one patients were tested at the end of treatment. One-third of these gave a more or less positive skin test with the 1:100 dilution but did not react to a more dilute solution of the pollen protein; the same number gave a more or less positive skin test with the 1:500 dilution, but failed to react to a more dilute pollen protein solution; one-half of these were given treatments with the 1:100 dilution, and the other half with the 1:500 dilution; a few were given only three doses of the 1:500 dilution; five failed to react at all with the 1:100 dilution, four were treated with the 1:100 dilution; one patient who was treated with the 1:100 dilution failed to react to the whole pollen; eight gave a more or less positive skin test with the 1:1,000 dilution, four having been treated with the 1:100 dilution without producing ill symptoms; two patients reacted with the 1:5,000 dilution of pollen protein—one, Patient 83, was shocked (urticaria) following the fifth treatment with a 1:500 dilution and was unimproved, whereas the other, Patient 178, had received two doses of the 1:100 dilution but was not

shocked and was 50 per cent. improved. Therefore, in all but two cases, treatment decreased the sensitivity of the patient, as evidenced by the skin test; or to be more specific, in practically three-fifths of the cases the intensity of the skin test diminished 100 times and in practically the remaining two-fifths it was decreased at least twenty times; the larger the number of treatments given, the greater was the decrease in the intensity of the skin test.

Pollens, other than ragweed, that might complicate the cause and treatment of hay-fever at this season of the year in New England have already been mentioned, and to a certain extent these have been eliminated. Since, however, a few patients listed in Table 1 did react rather strongly to other pollens, it may be advisable to mention them. Patients 4, 6, 23 and 29 gave more or less positive skin tests with a 1:1,000 dilution of daisy but the first two were free from symptoms and the other two were 75 per cent. benefited by six and four treatments, respectively, of a 1:500 dilution of ragweed pollen alone. Patient 26 reacted to a 1:1,000 dilution of corn pollen but was 75 per cent. improved by three doses of 1:500 dilution of ragweed pollen. Patients 19, 28 and 74 reacted more or less to a 1:1,000 dilution of goldenrod pollen, but following five treatments with 1:500 ragweed pollen. Patients 19 and 28 were free from symptoms, and Patient 74 was 75 per cent. benefited. Therefore, for reasons already stated, it would seem that pollens other than ragweed played no

part in the cause of hay-fever at this particular season.

The age at which hay-fever began, and the number of years that the patient has had hay-fever, seem to play no part in the cause or the treatment of this type of hay-fever. Neither does the sex of the patient have any bearing even on the frequency of the condition. The patients in Table 1 were equally divided between the two sexes. A number of the patients were treated at five-day intervals rather than, as was usually the case, at seven-day intervals. Altho statistics would not reveal any information on this point, it is my impression that the seven-day interval is preferable to the five-day interval. The individuality of the patient certainly plays a great part in the treatment and in the results of treatment of hay-fever; however, any definite information in regard to this point can not be obtained.

The same season in different years varies greatly in regard to the abundance of pollen, the beginning and the end of pollination and the frequency of colds that may be mistaken for hay-fever and thereby complicating the results of treatment. For example, in 1918, ragweed began to pollinate about August 8; 1918 and 1919, frosts sufficiently heavy to stop pollination occured about the middle of September, and even during all of September the weather was cold and rainy, so that not only was pollination below normal but head colds were frequent and the influenza epidemic was present. The season of

1920 was very favorable for ragweed; no frosts severe enough to injure it occurred, and pollination continued from about August 13 until October 1, at which time the plant naturally completed pollination and went to seed. There was no epidemic of colds and very little rain. For these reasons the results of preseasonal or preventive treatment with ragweed pollen in 1920 are of great value and are a true test for the treatment. Before considering these results, however, it should be noted that the amount of treatment given in this particular year was, in general, less than that given in preceding years. On referring to Table 1, season of 1920, the following are seen to have been the results of ragweed treatment; of the 115 patients treated, 27 per cent. experienced little or no hay-fever; 40 per cent. were 75 per cent. relieved; about 66 per cent. were, therefore, either 75 per cent. relieved or more so, and less than 33 per cent. had as little as 50 per cent. relief, whereas only three patients or 2.6 per cent., were not benefited by treatment.

Before Table 2 is discust, attention should be called to the plants that pollinate during June and July, the early hay-fever or so-called rose cold season. In the New England States some of the compositae, the most important of which is daisy, pollinate at this time, but for reasons already given daisy pollen rarely, if ever, is a cause of hay-fever. Such plants as the lilies, sorrel, buttercup and others pollinate at this time, but when tested no patient has been

found to be sensitive to these, and if they ever cause hay-fever it is because of immediate nasal contact with the blossom. The rose which pollinates at this time is rarely a cause of hay-fever since it is not a wind pollinated plant. Since, however, rose is commonly suspected to be the cause of hay-fever or rose colds, and since the pollen of rose is occasionally the actual cause, skin tests with rose pollen frequently have to be done, if for no other reason than to satisfy the patient. Altho in Table 2 only two patients (219 and 226) are represented as having been tested with rose pollen, thirty-three others of the fifty-two were tested with rose, and thirty-one failed to react more than doubtfully with the whole pollen of either the red or the white rose, and the two who did give a positive skin test with the whole pollen failed to react at all with a 1:100 dilution of the pollen. The thirty-five patients who were tested with rose pollen were tested with it because they thought roses caused their hay-fever, and the other patients in Table 2 were not tested with it because they were sure that roses did not cause their hay-fever. Therefore, it would seem that in New England roses were rarely the chief cause of hay-fever.

The cause of hay-fever during June and July in the New England States is practically limited to the pollens of the grass family. Lawn grass begins to pollinate early in May, as a rule, but since it is rare for hay-fever to begin early in May, lawn grass pollen is probably rarely, if

ever, the chief cause of hay-fever. Since, however, lawn grass continues to pollinate throughout the summer even when it is repeatedly mowed closely, with those patients who are sensitive to the pollens of other grasses and are either not treated or are insufficiently treated with the particular grass pollen that is the chief cause of hay-fever, exposure to lawn grass pollen may be a complicating cause or may aggravate the symptoms of hay-fever. Orchard grass pollinates during July, but this type of grass grows in more or less secluded places, and it is not commonly encountered. The same thirty-five patients who were tested with rose pollen were also tested with orchard grass pollen. Thirty of them failed to give positive skin tests with the whole pollen, and the five who gave a positive test with the whole pollen, failed to react with a 1:100 dilution of the pollen extract; therefore, orchard grass rarely, if ever, is an actual cause of hay-fever. Since corn is a member of the grass family, and since the table variety pollinates during July, it must be considered among the possible causes of early hay-fever. Forty of the fifty-two patients presented in Table 2 were tested with sweet corn pollen; twenty-two failed to react at all, and eighteen gave a positive skin test with the whole pollen, altho no tests with a 1:100 dilution of the pollen extract were positive. The large number of positive tests with the whole pollen was probably due, in part, at least, to the very large amount of protein present in corn pollen in

TABLE 2.—PRESEASONAL TESTS AND TREATMENTS WITH GRASS POLLENS

G = Good. F = Fair. N = None.

Patient	Age of Onset	Duration	Tests Before Treatment: Timothy	Red Top	June Grass
				Season 1917	
201	50	10	1-1,000±	1-1,000±	....
202	14	8	1-10,000±	1-1,000±	....
203	23	18	1-500±	1-1,000±	....
204	12	40	1-5,000+	1-1,000±	....
205	30	5	1-1,000+	1-1,000±	....
206	10	9	1-5,000±	1-100+	....
207	27	10	1-1,000±	1-500±	....
208	6	5	1-1,000+	1-100±	....
209	7	14	1-5,000±	1-5,000±	....
				Season 1918	
210	25	7	1-10,000±	1-5,000±	....
211	34	10	1-1,000±	1-5,000±	....
212	27	18	1-1,000±	1-1,000±	....
213	19	4	1-5,000+	1-1,000+	....
214	32	13	1-500±	1-500±	....
215	13	6	1-5,000±	1-500±	....
216	5	11	1-1,000+	1-100.0	....
				Season 1919	
217	20	15	1-5,000±	1-1,000±	1-1,000±
218	33	12	1-1,000+	1-1,000+	1-1,000+
220	7	2	1-5,000±	1-1,000±	1-5,000±
221	20	8	1-1,000+	1-1,000+	1-1,000+
222	..	..	1-5,000±	1-1,000±	1-1,000±
223	1	37	1-5,000±	1-5,000±	1-5,000±
224	8	3	1-1,000±	1-1,000±	1-1,000±
225	12	5	1-1,000±	1-500+	1-1,000±
				Season 1920	
227	9	2	1-5,000±	1-5,000±	1-5,000±
228	3	11	1-1,000±	1-1,000+	1-1,000+
229	23	4	1-5,000±	1-5,000+	1-1,000+
230	23	6	1-5,000±	1-5,000±	1-500+
231	8	5	1-10,000+	1-10,000+	1-5,000+
232	29	15	1-1,000+	1-1,000±	1-500±
233	11	3	1-10,000+	1-10,000+	1-10,000+
234	23	25	1-1,000±	1-1,000±	1-5,000±
235	21	30	1-10,000±	1-1,000+	1-5,000±
236	36	11	1-5,000+	1-1,000+	1-5,000+
237	13	4	1-1,000+	1-1,000+	1-1,000+
238	12	4	1-5,000±	1-5,000±	1-5,000+
239	20	2	1-500+	1-5,000±	1-1,000+
240	22	8	1-5,000±	1-5,000+	1-5,000+
241	15	12	1-1,000+	1-5,000±	1-5,000±
242	7	5	1-500+	1-500±	1-100±
242	6	40	1-5,000+	1-5,000±	1-5,000±
244	30	22	1-5,000+	1-5,000+	1-5,000+
245	19	1	1-1,000±	1-500±	1-1,000±

TABLE 2.—PRESEASONAL TESTS AND TREATMENTS WITH GRASS POLLENS (Continued)

Patient	Age of Onset	Duration	Tests Before Treatment		
			Timothy	Red Top	June Grass
246	1	20	Negative	1-1,000±	Negative
247	4	4	1-5,000+	1-1,000±	1-5,000+
248	..	4	1-5,000+	1-500±	1-1,000+
249	21	20	1-5,000±	1-1,000+	1-5,000+
250	16	19	1-5,000+	1-1,000+	1-5,000+
251	..	..	1-500±	1-100.0	1-500±
252	14	9	1-500±	1-500±	1-500±
219	..	3	1-1,000±	1-1,000±	1-1,000± Rose 1-500+
226	26	38	Negative	Negative	Rose 1-500+

comparison to the small amount of protein present in other pollens. Corn pollen is very heavy, it rapidly descends to the ground and is carried by air currents or wind only a few feet, therefore, intimate exposure would be required to produce symptoms; furthermore, only rarely would a person be unable to avoid it. Therefore, corn pollen must rarely, if ever, be considered a cause of hay-fever in the New England States where no large acreage exists in any locality as is the case in the West. This same statement is, likewise, true of wheat, oats, barley and rye.

The grasses, then, with which we are concerned in New England are June grass, Timothy and redtop, the pollens of which are light and are carried by wind considerable distances. June grass begins to pollinate some years as early as the middle of May; when the season is very late, it does not pollinate before the last day or two in May; pollination continues for about three weeks. Timothy and redtop begin

TABLE 2.—PRESEASONAL TESTS AND TREATMENTS WITH GRASS POLLENS (Continued)

G = Good. F = Fair. N = None.

Patient	Age of Onset	Duration	Number of Treatments with Final Dilution		
			Timothy	Red Top	June Grass
				Season 1917	
201	50	10	1-100:2	....	....
202	14	8	1-500:3	....	....
203	23	18	....	1-100:3	....
204	12	40	1-500:3	....	....
205	30	5	1-100:1	....	....
206	10	9	1-500:3	....	....
207	27	10	1-100:3	....	....
208	6	5	1-100:3	....	....
209	7	14	1-100:3	....	....
				Season 1918	
210	25	7	1-100:1	....	....
211	34	10	1-100:1	1-100:1	....
212	27	18	1-100:2	1-100:2	....
213	19	4	1-100:1	....	....
214	32	13	1-100:2	....	....
215	13	6	1-100:3	....	....
216	5	11	1-100:4	....	....
				Season 1919	
217	20	15	1-100:2	....	....
218	33	12	1-100:3	....	....
220	7	2	1-100:3	....	....
221	20	8	1-500:3	....	....
222	..	..	1-500:4	....	....
223	1	37	1-500:5	....	....
224	8	3	....	1-500:4	....
225	12	5	1-500:4	....	....
				Season 1920	
227	9	2	1-500:4	....	....
228	3	11	1-500:3	....	1-500:3
229	23	4	1-500:6	....	1-500:4
230	23	6	1-500:4	....	1-500:2
231	8	5	1-500:4	....	1-500:4
232	29	15	1-500:5	....	....
233	11	3	1-500:3	....	1-1,000:3
234	23	25	1-500:3	....	1-500:2
235	21	30	1-500:4	....	1-500:1
236	36	11	1-500:3	....	1-1,000:2
237	13	4	1-500:4	....	....
238	12	4	1-500:4	....	1-500:2
239	20	2	1 500:4	....	1-500:4
240	22	8	1-100:1	....	1-500:4
241	15	12	1-100:1	....	1-500:2
242	7	5	1-500:4	....	1-500:4
243	6	40	1-500:2	....	....
244	30	22	1-500:4	....	1-500:4

TABLE 2.—PRESEASONAL TESTS AND TREATMENTS WITH GRASS POLLENS (Continued)

Patient	Age of Onset	Duration	Number of Treatments with Final Dilution		
			Timothy	Red Top	June Grass
245	19	1	1-500:5	....	1-500:5
246	1	20	....	1-100:4	....
247	4	4	1-500:5	....	1-1,000:2
248	..	4	1-500:5	....	....
249	21	20	1-500:4	....	....
250	16	19	1-500:5	....	....
251	..	..	1-500:5	....	1-500:5
252	14	9	1-100:5	....	....
219	..	3	....	1-500:5	Rose 1-500:5
226	26	38	....	Negative	Rose 1-500:3

to pollinate between the middle of June and the first of July, depending on the season, and pollination continues until the middle or last of July; usually, the season of pollination lasts about six weeks. Therefore, in order to complete the schedule of treatments mentioned earlier in this paper as being desirable, preseasonal treatment with June grass must begin the first of March at the latest, and with timothy and redtop it must begin the middle of March.

Analysis of Table 2 shows the results of preseasonal treatment for the early type of hay-fever. Of the fifty-two patients treated, twenty-one, or 40.4 per cent., were free from symptoms; nine, or 17.3 per cent., were practically free from symptoms; ten, or 19.2 per cent., were 75 per cent. relieved; nine, or 17.3 per cent., were 50 per cent. relieved, and three, or 5.8 per cent., were not benefited. Twenty-eight of the patients were treated with timothy grass pollen alone, three with redtop alone, one with rose

TABLE 2.—PRESEASONAL TESTS AND TREATMENTS WITH GRASS POLLENS (Continued)

G = Good. F = Fair. N = None.

Patient	Age of Onset	Duration	Tests at End of Treatment			Result of Treatment
			Timothy	Red Top	June Grass	
				Season 1917		
201	50	10	....	....	....	G.
202	14	8	....	....	....	G.
203	23	18	....	....	....	50%
204	12	40	....	....	....	G.
205	30	5	....	....	....	75%
206	10	9	1-100.0	....	....	G.
207	27	10	1:100.0	....	....	G.
208	6	5	1-100 ±	....	....	G.
209	7	14	....	....	....	G.
				Season 1918		
210	25	7	....	....	....	G.
211	34	10	....	....	....	G.
212	27	18	....	....	....	G.
213	19	4	....	....	....	G.
214	32	13	....	....	....	G.
215	13	6	....	....	....	F.
216	5	11	....	....	....	G.
				Season 1919		
217	20	15	1-100 ±	1-1,000 ±	1-1,000 ±	G.
218	33	12	1-100 ±	1-500 ±	1-500 ±	G.
220	7	2	1-100 ±	1-500 +	1-500 +	G.
221	20	8	....	....	....	50%
222	..	..	....	....	....	G.
223	1	37	1-500 ±	1-500 ±	1-500 ±	G.
224	8	3	....	....	....	50%
225	12	5	....	....	....	F.
				Season 1920		
227	9	2	....	....	....	75%
228	3	11	....	....	....	75%
229	23	4	....	....	....	50%
230	23	6	....	....	....	75%
231	8	5	....	....	....	50%
232	29	15	....	....	....	50%
233	11	3	....	....	....	75%
234	23	25	....	....	....	50%
235	21	30	....	....	....	F.
236	36	11	....	....	....	50%
237	13	4	....	....	....	N.
238	12	4	....	....	....	50%
239	20	2	....	....	....	G.
240	22	8	....	....	....	75%
241	15	12	....	....	....	N.
242	7	5	....	....	....	F.
243	6	40	....	....	....	75%
244	30	22	....	....	....	F.

TABLE 2.—PRESEASONAL TESTS AND TREATMENTS WITH GRASS POLLENS (Continued)

Patient	Age of Onset	Duration	Tests at End of Treatment			Result of Treatment
			Timothy	Red Top	June Grass	
245	19	1	....	....	....	75%
246	1	20	....	....	....	F.
247	4	4	....	....	....	F.
248	..	4	....	....	....	N.
249	21	20	....	....	....	75%
250	16	19	....	....	....	75%
251	..	..	....	....	....	F.
252	14	9	....	....	....	G.
219	..	3	....	....	....	F.
226	26	38	....	....	....	G.

alone, two with timothy and redtop together, one with redtop and rose together and seventeen with timothy and June grass pollens together. Altho these facts are of interest, much valuable information is missed unless particular attention is given to each year; therefore, each year will be discust separately.

During the season 1917, nine patients were treated. Only one patient (203) was treated with redtop pollen, because this patient was more sensitive to dilutions of redtop pollen extract than to timothy pollen extract; the remaining eight patients were treated with timothy pollen extract alone because all but two were more sensitive to timothy pollen extract than to redtop pollen extract, and since these two were equally sensitive to both pollen extracts, timothy was selected for treatment because it was thought that timothy was more prevalent than redtop. Judging from the excellent results and the decreased sensitivity of the patients, there is every

reason to believe that all patients had a sufficient number of treatments, that all but two, who were 50 and 75 per cent., respectively, relieved by treatment with redtop pollen extract, were treated by the proper pollen. As a matter of fact, the two patients who were only 50 per cent. and 75 per cent. relieved had most of their symptoms during June rather than in July which fact would make one suspicious that some pollen other than those tested was the cause of symptoms; tests were made with orchard grass, corn and rose, none of which reacted in a dilution of 1 : 100, but June grass, which also pollinates during June, was not tested. With the exception of these two cases, timothy pollen extract would seem to have protected against redtop exposure since five of the patients were very sensitive to redtop pollen extract.

During 1918, seven patients were treated, and all but one were free from symptoms and that one was practically free. All patients were treated one or more times with the 1 : 100 dilution and all but two were treated with timothy pollen extract alone; these two were treated with the extracts of timothy and redtop pollens together. Therefore, the same conclusions that were drawn from the 1917 series hold true for the 1918 series, namely, that all patients had a sufficient number of treatments, that treatment with timothy pollen extract protects against redtop exposure, that, as a rule, patients are more sensitive to timothy pollen than to any other pollen prevalent at that time, with the possible exception of

June grass which was not tested, and that the reason why two patients were treated with redtop pollen in addition to timothy pollen was because one was more sensitive to redtop than to timothy and the other was equally sensitive to both.

During 1919, eight patients were treated with the result that five were free from symptoms, one other was practically free, and two were only 50 per cent. relieved. Of the two patients (221 and 224) who were only 50 per cent. benefited, one had only three treatments with timothy pollen extract 1:500 and the other was treated with redtop instead of timothy; both patients had more symptoms in June than in July. Therefore, as regards timothy and redtop the same conclusions that were true of 1917 and 1918 were equally true for 1919. In 1919, tests were made with June grass and on referring to the table, season 1919, it will be seen that the eight patients reacted as strongly to June grass pollen as to redtop; some reacted more strongly to it, and all but two were as sensitive to June grass as to timothy pollen extract. It is also noted that four patients, who were tested with the three grass pollens at the end of timothy pollen treatment, showed a much greater decrease in sensitiveness to timothy pollen than to redtop or to June grass pollen. Therefore, since there is evidence that timothy pollen treatment seems to protect against redtop pollen exposure, as has already been shown, and since the patients in 1917 and 1919 who were least benefited

by treatment, either by timothy or redtop, had most of their symptoms during the usual time of June grass pollination rather than during the time that timothy and redtop pollinate, and since in 1919 it was shown that early hay-fever patients are very sensitive to June grass pollen extract, it was deemed best to treat suitable patients with June grass pollen during 1920.

During the 1920 season, only three of twenty-eight patients were to any extent less sensitive to June grass pollen extract than to timothy pollen extract, and three of the patients were more sensitive to June grass pollen than to timothy. Therefore, in seventeen patients treatment was given with June grass pollen extract together with timothy pollen extract. The results of this mixed treatment were: One patient was free from symptoms, five were practically free, five were 75 per cent. relieved, five were 50 per cent. relieved, and one was not benefited; a very poor showing as compared to treatment with timothy pollen extract alone during the three previous years. It is also noted that only two patients who were treated with the mixture were given as many as one treatment with timothy, 1:100, which is desirable and which was the case in previous seasons when excellent results were obtained; treatment with a mixture of the two pollens did not and will not permit of sufficient treatment with either one, and in this instance it is evident that a part, at least, of the poor results, if the three former seasons are a guide, was due to insuffi-

cient treatment with timothy pollen. The absence of treatment with redtop pollen can not explain the poor results, since in the three former seasons excellent results were obtained in the absence of redtop treatment.

Special attention is called to Patients 246, 219 and 226 because their cases are of considerable interest. Patient 246 was sensitive to redtop pollen alone and was practically free from symptoms following four treatments with the 1:100 dilution of redtop pollen extract. Not only was this patient free from symptoms while in New England, but he was also free while in Wyoming and was practically free while in California. Patient 219, who was practically equally sensitive to the pollens of the three grasses and to rose, was practically free from symptoms following treatment with equal parts of redtop and rose pollen extracts. Patient 226, who was sensitive to rose pollen only, was free from symptoms following treatment with rose pollen extract. Therefore, only two rose cases were encountered in the four seasons during which fifty grass cases were tested and treated.

My conclusions, based on a four years' experience with the treatment of June and July hay-fever, are: While the pollen of timothy grass is the chief cause of hay-fever, and sufficient treatment with it alone gives excellent results, it is necessary to test all patients with the pollens of redtop, June grass and rose since an occasional patient is more sensitive to one of these pollens than to timothy pollen, and,

therefore, such a patient may need treatment with one of them rather than with timothy pollen. When the same patient, as is frequently the case, is equally sensitive to the dilutions of the pollen extracts of timothy, redtop and June grass, it is advisable to treat the patient with timothy pollen extract alone because there is sufficient evidence that treatment with timothy pollen will protect against redtop pollen exposure, provided one or more treatments are given with the 1:100 dilution of the pollen extract; timothy and redtop pollinate at the same time, and redtop is less prevalent than timothy. Sufficient treatment with timothy pollen extract seems to protect also against June grass pollen exposure, but since, as is often the case, June grass pollination is well advanced or even sometimes completed before timothy pollination begins, the patients being treated with timothy have not had sufficient treatment with timothy pollen to protect them completely against June grass pollen, consequently some of these patients will have more or less symptoms from June grass exposure, as happened in 1917 with Patients 203 and 205; in 1919, with Patients 221 and 224, and in 1920 with Patients 232 and 249. In 1918, when June grass pollination was late, timothy treatment was successful, and the few cases in Table 2 that were tested with the three grass pollens at the end of much timothy treatment alone, were considerably less sensitive to all of the grass pollens and all of the patients were free from symptoms. Unless treatment with June grass

TABLE 3.—INSUFFICIENT POLLEN TREATMENT

N = None. F = Fair.

Patient	Age of Onset	Duration	Tests Before Treatment	Number of Treatments with Final Dilution	Result of Treatment
Ragweed					
253	32	13	1-10,000 +	1-1,000:2	N.
254	22	4	1-5,000 ±	1-1,000:3	50%
255	3	10	1-5,000 ±	1-1,000:3	75%
256	18	5	1-1,000 ±	1-1,000:3	50%
257	14	24	1-5,000 ±	1-1,000:2	50%
258	16	45	1-5,000 ±	1-1,000:2	50%
259	19	15	1-5,000 ±	1-1,000:2	25%
260	28	14	1-1,000 +	1-1,000:2	75%
261	13	9	1-5,000 ±	1-1,000:3	50%
262	39	10	1-5,000 +	1-1,000:3	N.
263	31	2	1-1,000 ±	1-500:2	N.
264	3	9	1-10,000 +	1-5,000:4	N.
265	6	12	1-10,000 +	1-1,000:2	50%
266	16	7	1-10.000 ±	1-1,000:3	75%
267	44	10	1-10,000 ±	1-5,000:5	50%
289	16	45	1-10,000 ±	1-500:2	50%
268	27	12	1-10,000 ±	1-500:2	50%
269	44	6	1-5,000 +	1-500:2	50%
271	14	9	1-5,000 ±	1-1,000:2	N.
272	9	2	1-5,000 ±	1-5,000:5	50%
273	14	10	1-5,000 +	1-500:2	N.
274	29	3	1-10,000 ±	1-5,000:1	50%
275	3	49	1-10,000 ±	1-500:2	N.
276	3	6	1-20,000 ±	1-5,000:3	50%
277	9	9	1-10,000 ±	1-500:2	50%
278	3	20	1-10,000 ±	1-5,000:4	50%
279	16	16	1-10,000 ±	1-500:1	N.
280	5	19	1-10,000 ±	1-1,000:2	50%
281	18	3	1-10,000 ±	1-500:2	75%
282	35	12	1-10,000 ±	1-1,000:2	F.
283	31	6	1-10,000 ±	1-500:2	75%
284	35	15	1-10,000 ±	1-500:2	50%
285	13	16	1-1,000 +	1-500:2	75%
294	11	7	1-5,000 ±	1-500:2	50%
295	31	5	1-5,000 ±	1-500:2	N.
296	20	17	1-5,000 ±	1-500:1	50%
297	22	25	1-5,000 ±	1-500:2	75%
298	11	7	1-5,000 ±	1-500:2	50%
299	37	18	1-5,000 ±	1-500:2	50%
270	41	7	1-5,000 ±	1-500:2	50%
Timothy					
286	30	4	1-5,000 ±	1-1,000:2	N.
287	19	10	1-10,000 ±	1-5,000:3	N.
288	30	5	1-5,000 ±	1-1,000:3	50%
290	14	6	1-5,000 ±	1-1,000:2	N.
291	8	3	1-1,000 ±	1-500:2	50%
292	14	14	1-10,000 ±	1-500:2	N.
293	22	5	1-10,000 ±	1-5,000:5	50%

pollen is begun earlier than is customary with timothy pollen, patients will not be treated sufficiently with June grass pollen. Therefore, treatment with both timothy pollen and June grass pollen extracts together will not only be insufficient to protect against early June grass pollination (Patients 229, 233, 234 and 238, all of whom had symptoms in late May and early June), but the combination of the two pollen extracts necessarily retards and diminishes the amount of treatment that might be given with timothy alone. Table 2 shows this to be the usual case. Therefore, I am opposed to preseasonal treatment with pollen mixtures, except on rare occasions, and in the case of June grass it is better to take a chance on a late season with timothy protection, or even an early season with few symptoms, than to treat with it in conjunction with timothy when timothy treatment is essential.

In Table 3 are presented patients who had insufficient pollen treatment, and by insufficient is meant that for some reason or other the complete schedule of treatments, as outlined early in this paper, could not be given. A few of the patients did receive the 1:500 dilution of the pollen extract two times, but for reasons already stated I consider this insufficient treatment.

In Table 3 are presentel forty patients who were given insufficient treatment with ragweed pollen extract, and seven patients similarly treated with timothy pollen extract. The possibility of sensitization to pollens, that might be the cause of symptoms, other than ragweed

and timothy will not be considered in the light of previous discussion. The results were as follows: Of the forty-seven patients in Table 3, none were free from symptoms, one was practically free, seven were 75 per cent. benefited, twenty-five were 50 per cent. benefited, one was 25 per cent. benefited and the remaining thirteen were not benefited. Therefore, altho a few patients may be from 50 to 75 per cent. benefited by as small a number as two treatments of the 1 : 500 dilution, these results are offset by the number of failures resultant from similar treatment, and this is still more evident when a smaller amount of treatment than two doses of the 1 : 500 dilution is given. The results shown in Table 3 verify what has already been proven in Tables 1 and 2, namely, that giving less than three preseasonal treatments with the 1 : 500 dilution of pollen extract is undesirable.

In table 4 are presented seventy-three patients who were treated with ragweed pollen extract two years in succession. Six patients were treated in the two seasons 1917 and 1918; fifteen, in 1918 and 1919, and fifty-two in 1919 and 1920.

Analysis of Table 4 shows that for the first year of treatment, of the seventy-three patients, twenty-eight, or 38+ per cent., were free from symptoms; sixteen, or 22 per cent., were practically free; fourteen, or 19+ per cent., were 75 per cent. relieved; twelve, or 16.4 per cent., were 50 per cent. benefited, and three, or 4+ per cent., were not benefited. For the second

TABLE 4.—PRESEASONAL TESTS AND TREATMENT WITH RAGWEED POLLEN TWO SUCCESSIVE YEARS

G = Good. F = Fair. N = None.

Patient	Age of Onset	Duration	Season 1917				Season 1918			
			Tests Before Treatment	Number Treatments with Final Dilution	Tests at End of Treatment	Result of Treatment	Tests Before Treatment	Number Treatments with Final Dilution	Tests at End of Treatment	Result of Treatment
300	16	10	1-1,000 ±	1-100:2	....	G.	1-1,000 ±	1-100:2	....	G.
301	..	10	1-1,000 ±	1-100:3	....	G.	1-5,000 ±	1-100:1	1-500 ±	G.
302	45	3	1-5,000 ±	1-100:1	....	G.	1-500 ±	1-500:5	....	G.
303	39	10	1-5,000 +	1-500:4	....	G.	1-5,000 +	1-100:2	....	G.
304	20	10	1-5,000 ±	1-100:3	....	G.	1-5,000 ±	1-500:5	....	75%
305	32	6	1-5,000 +	1-500:4	....	75%	1-1,000 +	1-100:1	....	G.
			Season 1918				Season 1919			
306	24	25	1-5,000 ±	1-500:5	....	G.	1-5,000 ±	1-500:5	....	75%
307	14	15	1-5,000 ±	1-100:2	....	G.	1-5,000 ±	1-100:4	1-100 +	G.
308	42	8	1-5,000 ±	1-500:5	....	50%	1-5,000 +	1-100:3	1-100 +	75%
309	37	9	1-1,000 +	1-500:8	....	G.	1-5,000 ±	1-100:3	1-100 ±	G.
310	3	10	1-5,000 ±	1-500:3	....	G.	1-5,000 +	1-500:4	....	G.
311	20	25	1-5,000 ±	1-100:4	....	N.	1-5,000 ±	1-100:1	....	N.
312	6	26	1:5,000 +	1-100:1	....	G.	1-5,000 ±	1-100:5	1-500	G.
314	3	11	1-5,000 ±	1-500:7	....	75%	1-10,000 ±	1-500:4	....	N.
315	13	3	1-5,000 ±	1-500:4	....	50%	1-10,000 ±	1-500:3	....	F.
316	34	9	1-5,000 +	1-500:7	....	75%	1-5,000 +	1-100:2	....	N.
317	37	4	1-1,000 ±	1-500:2	....	50%	1-1,000 +	1-500:4	1-100 ±	75%
318	12	2	1-5,000 ±	1-500:2	....	50%	1-5,000 ±	1-100:4	1-100 ±	75%

TABLE 4.—PRESEASONAL TESTS AND TREATMENT WITH RAGWEED POLLEN TWO SUCCESSIVE YEARS (Continued)

G = Good. F = Fair. N = None.

Patient	Age of Onset	Duration	Season 1918				Season 1919			
			Tests Before Treatment	Number Treatments with Final Dilution	Tests at End of Treatment	Result of Treatment	Tests Before Treatment	Number Treatments with Final Dilution	Tests at End of Treatment	Result of Treatment
319	13	16	1-1,000 +	1-500:5	....	F.	1-1,000 +	1-500:2	....	75%
320	29	6	1-5,000 ±	1-100:4	....	N.	1-10,000 ±	1-100:3	....	50%
321	23	4	1-1,000 +	1-500:6	....	75%	1-5,000 ±	1-500:4	1-100.0	75%
			Season 1919				Season 1920			
322	32	10	1-5,000 +	1-100:4	1-100 ±	G.	1-5,000 ±	1-500:3	....	75%
323	39	5	1-10,000 ±	1-100:4	1-100 +	F.	1-5,000 +	1-100:1	1-500 ±	75%
324	29	4	1-5,000 +	1-100:4	1-100 +	G.	1-5,000 ±	1-500:5	....	75%
325	..	..	1-1,000 ±	1-100:4	1-100 +	F.	1-1,000 +	1-500:3	....	75%
326	50	2	1-5,000 ±	1-100:5	1-500 ±	G.	1-1,000 +	1-100:2	1-500 ±	75%
327	..	..	1-10,000 ±	1-100:5	1-500 +	G.	1-10,000 ±	1-500:5	....	G.
328	18	3	1-5,000 ±	1-500:5	1-100 ±	G.	1-5,000 ±	1-100:2	....	75%
329	..	..	1-5,000 ±	1-500:5	....	G.	1-5,000 ±	1-100:3	....	F.
330	34	10	1-5,000 +	1-100:5	1-100.0	N.	1-1,000 ±	1-100:3	....	75%
331	14	7	1-10,000 ±	1-500:5	....	50%	1-10,000 ±	1-100:3	....	75%
322	12	9	1-5,000 ±	1-500:5	....	F.	1-1,000 ±	1-500:5	....	75%
333	4	12	1-10,000 ±	1-500:5	....	75%	1-10,000 ±	1-500:5	....	F.
334	10	7	1-10,000 ±	1-100:2	1-500 ±	F.	1-10,000 ±	1-500:4	....	F.
335	19	12	1-5,000 ±	1-500:4	....	75%	1-5,000 ±	1-100:1	1-5,000 ±	50%
336	32	12	1-10,000 ±	1-100:3	1-500 ±	75%	1-10,000 ±	1-500:4	....	50%

TABLE 4.—PRESEASONAL TESTS AND TREATMENT WITH RAGWEED POLLEN TWO SUCCESSIVE YEARS (Continued)

G = Good. F = Fair. N = None.

Patient	Age of Onset	Duration	Season 1919				Season 1920			
			Tests Before Treatment	Number Treatments with Final Dilution	Tests at End of Treatment	Result of Treatment	Tests Before Treatment	Number Treatments with Final Dilution	Tests at End of Treatment	Result of Treatment
337	17	25	1-20,000 ±	1-100:2	....	G.	1-10,000 ±	1-100:1	1-500 ±	F.
338	..	36	1-10,000 ±	1-500:6	....	G.	1-5,000 +	1-500:5	....	F.
339	32	10	1-10,000 ±	1-100:4	1-100 +	F.	1-5,000 ±	1-100:3	....	75%
340	..	25	1-10,000 +	1-500:4	....	F.	1-5,000 ±	1-500:5	....	75%
341	30	15	1-5,000 +	1-500:6	1-100.0	75%	1-5,000 +	1-500:2	....	50%
342	30	4	1-10,000 +	1-100:2	1-500 +	F.	1-10,000 ±	1-500:4	....	50%
343	32	6	1-20,000 ±	1-100:3	1-500 ±	F.	1-10,000 ±	1-500:4	....	F.
344	5	2	1-10,000 ±	1-100:2	....	G.	1-1,000 ±	1-100:2	....	G.
345	4	34	1-10,000 ±	1-100:2	1-500 ±	75%	1-5,000 ±	1-100:2	1-500 ±	F.
346	6	4	1-10,000 ±	1-500:4	1-500 ±	75%	1-5,000 ±	1-500:6	1-500.0	75%
347	14	5	1-5,000 ±	1-500:6	1-500 +	F.	1-5,000 ±	1-500:5	1-500 +	50%
348	16	45	1-10,000 ±	1-500:2	1-1,000 +	50%	1-10,000 ±	1-500:5	1-1,000 +	F.
349	28	10	1-10,000 ±	1-500:6	....	G.	1-5,000 +	1-500:6	....	F.
350	27	6	1-10,000 ±	1-100:4	1-100 +	F.	1-5,000 +	1-500:5	....	50%
351	5	19	1-10,000 ±	1-500:3	....	75%	1-10,000 ±	1-1,000.1	....	F.
352	18	5	1-10,000 +	1-500:4	1-500 ±	75%	1-5,000 ±	1-500:4	....	75%
353	27	7	1-20,000 ±	1-100:3	1-500 ±	F.	1-10,000 ±	1-500:3	....	75%
354	38	4	1-5,000 ±	1-100:4	1-500 ±	F.	1-5,000%	1-100:1	1-500 +	F.
355	34	12	1-10,000 ±	1-500:5	....	75%	1-5,000 ±	1-500:5	....	75%
356	28	6	1-20,000 ±	1-500:4	....	G.	1-5,000 ±	1-500:5	....	F.

TABLE 4.—PRESEASONAL TESTS AND TREATMENT WITH RAGWEED POLLEN TWO SUCCESSIVE YEARS (Continued)

G = Good. F = Fair. N = None.

Patient	Age of Onset	Duration	Season 1919				Season 1920			
			Tests Before Treatment	Number Treatments with Final Dilution	Tests at End of Treatment	Result of Treatment	Tests Before Treatment	Number Treatments with Final Dilution	Tests at End of Treatment	Result of Treatment
357	5	36	1-10,000 ±	1-100:1	1-500 ±	50%	1-5,000 ±	1-500:5	....	F.
358	28	13	1-10,000 ±	1-500:5	1-500 ±	50%	1-20,000 ±	1-500·4	....	50%
359	..	28	1-20,000 +	1-500:1	....	50%	1-20,000 +	1-500·5	1-1,000 +	75%
360	23	39	1-20,000 ±	1-100:5	1-500 ±	F.	1-10,000 ±	1-100:3	....	F.
361	45	7	1-1,000 ±	1-100:1	1-100 +	G.	1-5,000 ±	1-500:4	1-500.0	75%
362	29	9	1-5,000 ±	1-500:5	1-500 +	50%	1-10,000 ±	1-500·5	....	75%
363	18	10	1-10,000 ±	1-500:4	1-500 ±	G.	1-5,000 ±	1-500:5	....	F.
364	27	20	1-10,000 ±	1-500:4	....	75%	1-5,000 +	1-500:5	....	75%
365	31	28	1-5,000 ±	1-500:3	....	F.	1-5,000 ±	1-500:3	....	50%
366	25	3	1-10,000 +	1-500·4	1-500 +	50%	1-10,000 ±	1-500:6	1-500 +	75%
367	33	5	1-1,000 ±	1-100:4	1-100.0	G.	1-500 ±	1-500:4	....	75%
313	1	3	1-5,000 +	1-500 5	....	G.	1-5,000 ±	1-100:2	....	G.
368	40	18	1-10,000 ±	1-100:1	1-100 ±	G.	1-5,000 +	1-500:5	....	75%
369	11	8	1-5,000 +	1-500:5	1-500 ±	F.	1-5,000 ±	1-500:5	....	7
370	14	18	1-5,000 ±	1-100:4	1-100 ±	G.	1-500 ±	1-100:2	1-100 ±	75%
371	32	31	1-10,000 +	1-100:4	1-100 +	G.	1-5,000 ±	1-100:2	1-500 ±	75%
372	7	6	1-10,000 ±	1-100:1	1-100 ±	50%	1-5,000 ±	1-500:6	....	75%

year of treatment, the results were: Of the seventy-three patients, twelve, or 16.4 per cent., were free from symptoms; sixteen, or 22 per cent., were practically free; thirty-three, or 45 per cent., wer 75 per cent. relieved; nine, or 12 per cent., were 50 per cent. relieved, and three, or 4+ per cent., were not benefited. On comparing the results obtained from the first year's treatment with those obtained from the second year's treatment, it is noted that the same number of patients were practically free from symptoms both years, and that the number who were 50 per cent. benefited were about the same for the year, but that there were 57 per cent. more all right the first year than the second year, and 57 per cent. more that were 75 per cent. benefited the second year than the first.

Altho the above results obtained by the first and second years' treatment do not differ markedly, yet this difference shows rather poorer results from the second year's treatment than from the first year's treatment, the opposite of what one would expect and desire. By comparing the amount of treatment that was given the first year with that given the second year it is evident that a diminished amount of treatment during the second year would seem to explain the poorer results obtained during this year, and it may be stated, that, as a rule, it is desirable to give as much treatment with the final dilutions the second year, provided sufficient treatment is given the first year, and sometimes less treatment is required.

Attention should be called to the few patients in Table 4 who were not benefited by treatment. Patient 311 was treated four times with the 1:100 dilution of pollen extract the first year, and once with the same dilution the second year, and yet there was no benefit from treatment either year; altho this patient was much worse during August and September, he did have symptoms throughout the year so that it is probable that there was some cause of hay-fever besides ragweed pollen. It is difficult to understand why Patient 314 should be 75 per cent. benefited following seven treatments with a 1:500 dilution of pollen extract the first year and not benefited by four similar treatments the second year unless the failure was due to insufficient treatment the second year. There is no evident reason why Patient 316, who was similarly treated both years, was 75 per cent. benefited the first year and not benefited the second year; neither is there an evident explanation why Patient 320, who was similarly treated both years, was not benefited the first year even tho at the end of treatment the skin test was negative with a 1:100 dilution of the pollen, but was 75 per cent. benefited the second year. It happens that all of these failures occurred during the two years 1918 and 1919, and both ragweed seasons, as already described, were very similar. None of these patients were sensitive to pollens other than ragweed.

Fifty-seven skin tests were done at the end of treatment. In one case (335) the test was the

same at the end of treatment as before treatment, and the patient was only 50 per cent. benefited; a similar instance was noted in Table 1. Patient 348 gave a positive skin test with a 1:1,000 dilution of the pollen extract both years at the end of treatment, but was 50 per cent. benefited the first year and was practically free from symptoms the second year. In the remaining fifty-four tests, there was the usual diminished intensity of the reaction; in one-third of the cases, or those who had been treated with the 1:100 dilution of pollen extract, the skin test was positive in no dilution higher than 1:100, and in some cases even this dilution was negative; in the remaining two-thirds of the instances no dilution higher than 1:500 gave a positive skin test at the end of treatment. The sensitivity of the patients was decreased from ten to one hundred times with an average decrease of from twenty to fifty times.

The conclusions resulting from Table 4 substantiate all of those already mentioned, and the conclusion that one or more treatments with a 1:100 dilution produces the best results and the greatest reduction in the intensity of the skin test is likewise confirmed.

In Table 5 are presented seven cases of early hay-fever treated two years in succession. During 1918 and 1919, three patients were treated with grass pollen; during 1919 and 1920 three patients were treated with grass pollen, and during 1917 and 1918 one patient was treated with rose pollen.

Patient 374, who was treated three times with a 1: 500 dilution of timothy pollen extract, was 75 per cent. benefited; what symptoms this patient had were present chiefly in early June. The second year, altho it was found that this patient was as sensitive to the pollen of June grass as to timothy, it was decided to treat him more strenuously with timothy pollen extract again since the first year's treatment with timothy was not deemed sufficient. Following two treatments with the 1: 100 dilution of timothy pollen extract the second year, he was again 75 per cent. benefited and again his chief symptoms were manifested in June. Therefore, it is quite evident that since his chief symptoms were manifested in early June, previous to timothy pollination and during the pollination of June grass, to which he was very sensitive, that June grass was the cause of the symptoms, and that altho timothy treatment had not protected against June grass, it was really successful as far as timothy was concerned. During a third year, 1920, he was treated only with June grass pollen extract and had no symptoms during June grass pollination, but he did have considerable trouble during late June and July. In order to simplify the table this treatment is omitted. Therefore, there is no question that during the 1918 and 1919 seasons his 25 per cent. of symptoms were caused by June grass pollen and that his timothy pollen treatment was successful. Patient 375 was treated four times each year with a

TABLE 5.—PRESEASONAL TESTS AND TREATMENT WITH GRASS POLLENS

TWO SUCCESSIVE YEARS

G = Good.

Patient	Duration	Age of Onset	Tests Before Treatment			Number Treatments With Final Dilution, Timothy	Tests at End of Treatment			Result of Treatment
			Timothy	Red Top	June Grass		Timothy	Red Top	June Grass	
Season 1918										
374	1	47	1-5,000 +	1-500 +	....	1-500:3	....	....	....	75%
375	19	10	1-5,000 ±	1-500 +	....	1-500:4	....	....	....	75%
376	22	12	1-5,000 ±	1-5,000 ±	....	1-500:4	....	....	....	G.
Season 1919										
377	11	8	1-5,000 ±	1-500 +	1-100 ±	1-100:1	1-100 +	....	....	G.
378	25	3	1-5,000 ±	1-1,000 ±	1-500 ±	1-100:5	1-100 ±	1-500 ±	1-100 ±	G.
379	11	3	1-5,000 ±	1-500 +	1-5,000 ±	1-100:3	....	....	....	G.
Season 1917										
373	21	3	Rose 1-1,000 +	—	—	Rose 1-500:5	....	....	....	G.

TABLE 5.—PRESEASONAL TESTS AND TREATMENT WITH GRASS POLLENS

TWO SUCCESSIVE YEARS (Continued)

G = Good.

Patient	Duration	Age of Onset	Season 1919								Result of Treatment
			Tests Before Treatment			No. Treatments with Final Dilution		Tests at End of Treatment			
			Timothy	Red Top	June Grass	Timothy	June Grass	Timothy	Red Top	June Grass	
374	1	47	1-5,000 ±	1-1,000 ±	1-5,000 ±	1-100:2	....	1-500 ±	1-1,000 ±	1-1,000 ±	75%
375	19	10	1-1,000 +	1-1,000 ±	1-500 ±	1-500:4	....	....	....	....	75%
376	22	12	1-1,000 ±	1-1,000 ±	1-500 ±	1-100:3	....	1-100 ±	1-100 +	1-100 +	G.
						Season	1920				
377	11	8	1-5,000 ±	1-500 ±	1-5,000 ±	1-500:4	1-1,000:2	....	....	....	75%
378	25	3	1-5,000 +	1-5,000 ±	1-5,000 ±	1-500:4	1-500:1	....	....	....	75%
379	11	3	1-5,000 ±	1-1,000 +	1-5,000 ±	1-500:5	1-1,000:3	....	....	....	50%
						Season	1918				
373	21	3	Rose 1-1,000 ±	....	....	Rose 1-500:6	....	....	....	....	G.

1:500 dilution of timothy pollen alone and was 75 per cent. benefited. Since this patient was not very sensitive to June grass and had no symptoms until timothy pollination, it is evident that he had, as already shown, insufficient timothy treatment. Patient 376 was chiefly sensitive to timothy pollen and was free from symptoms following treatment with timothy pollent extract.

Patients 377 and 378 were chiefly sensitive to timothy pollen extract the first year and were free from symptoms following treatment with timothy pollen alone. The second year they were equally sensitive to the pollens of both June grass and timothy, and were given less treatment than the preceding year with timothy pollen and a little treatment with June grass pollen extract; they were only 75 per cent. benefited the second year and their symptoms were manifested chiefly in late June and July. Therefore, treatment with the two pollen extracts together diminished the amount of treatment that they might have had with timothy alone, and the result was that both patients were only 75 per cent. benefited the second year; furthermore, it is evident that they did not need June grass pollen treatment any way. The case of Patient 379 was similar to the two cases just discust, with the exception that this patient was equally sensitive to both pollens the first year as well as the second year, and that she was only 50 per cent. benefited the second year by treatment similar to that given

the two cases just cited; the fact that this patient began treatment late, thus necessitating a five-day interval between treatments, may partly explain the poor results.

Patient 373 was sensitive to the pollen of rose alone, and five and six treatments in 1917 and 1918, respectively, prevented any symptoms both years even tho, since she was a nurse in a hospital, she had to be exposed freely to roses. Incidentally, it should be stated that previous to treatment, whenever she scratched her hands on rose thorns, marked itching and swelling resulted at the points of injury, but following rose pollen treatment these symptoms did not occur when injured by rose thorns.

The conclusions to be drawn from Table 5 verify those already proven correct in Table 2. The important conclusions are, that treatment with two pollens together is not advisable; that the early type of hay-fever is chiefly due to timothy pollen, and sufficient treatment with timothy pollen alone, namely, treatment with the 1:100 dilution or its equivalent of a 1:500 dilution, will give satisfactory results in such cases; that this amount of treatment will usually markedly diminish the intensity of the skin test to timothy pollen, and that only an occasional case of early hay-fever is due to rose pollen. The correctness of the conclusion drawn from Table 4 that usually the patient needs as much treatment with the final dilutions the second year as he received the first year is also proven.

In Table 6, twenty-five patients, who were

treated three years in succession with ragweed pollen extract, are presented. During 1917 to 1919 inclusive, five patients were treated, and during 1918 to 1920 inclusive, twenty were treated.

Analysis of Table 6 shows that following the first year of treatment, a third of the patients were free from symptoms; one patient, or 4

TABLE 6.—PRESEASONAL TESTS AND TREATMENT WITH RAGWEED POLLEN THREE SUCCESSIVE YEARS

G = Good. F = Fair.

Patient	Age of Onset	Duration	Season 1917		
			Tests Before Treatment	Number Treatments with Final Dilution	Result of Treatment
381	38	11	1-1,000±	1-100:1	G.
382	15	17	1-10,000±	1-500:3	75%
383	20	10	1-5,000±	1-100:3	G.
384	32	10	1-1,000+	1-100:2	G.
385	25	8	1-1,000+	1-100:3	G.
				Season 1918	
386	9	3	1-1,000±	1-500:3	G.
387	21	5	1-10,000±	1-100:1	75%
388	28	15	1-5,000±	1-500:3	50%
389	..	23	1-5,000±	1-500:3	75%
390	17	2	1-1,000±	1-500:2	50%
391	1	34	1-5,000+	1-500:5	75%
392	20	20	1-5,000+	1-100:2	75%
393	27	5	1-5,000±	1-500:3	75%
394	12	20	1-5,000±	1-500:4	G.
395	11	39	1-5,000±	1-500:3	75%
396	21	19	1-5.000+	1-500:4	G.
397	24	20	1-5,000±	1-500:4	F.
398	28	10	1-5,000±	1-500:5	75%
399	30	25	1-10,000±	1-500:6	50%
400	24	10	1-5,000±	1-500:4	50%
401	33	16	1-5,000±	1-500:2	50%
402	26	8	1-10 000±	1-500:3	75%
403	16	2	1-10,000±	1-500:2	50%
404	36	6	1-1,000+	1-100:4	G.
405	8	22	1-1,000+	1-100:1	G.

TABLE 6.—PRESEASONAL TESTS AND TREATMENT WITH RAGWEED POLLEN THREE SUCCESSIVE YEARS

(Continued)

G = Good. F = Fair.

Patient	Age of Onset	Duration	Season 1918			
			Tests Before Treatment	Number Treatments With Final Dilution	Tests After Treatment	Result of Treatment
381	38	11	1-1,000±	1-100:4	....	F.
382	15	17	1-10,000±	1-500:3	....	75%
383	20	10	1-5,000±	1-500:5	....	75%
384	32	10	1-1,000±	1-500:4	....	G.
385	25	8	1-1,000±	1-100:1	....	G.
				Season	1919	
386	9	3	1-500±	1-100:6	1-100.0	G.
387	21	5	1-10,000±	1-100:2	1-100+	F.
388	28	15	1-5,000±	1-100:2	1-100+	G.
389	..	23	1-5,000±	1-100:4	1-100+	G.
390	17	2	1-5,000±	1-100:5	1-100±	F.
391	1	34	1-5,000+	1-500:6	....	F.
392	20	20	1-10,000+	1-100:3	1-100+	G.
393	27	5	1-5,000±	1-100:3	1-100.0	G.
394	12	20	1-5,000±	1-100:1	1-500±	F.
395	11	39	1-5,000+	1-500:3	1-500+	75%
396	21	19	1-5,000+	1-500:4	1-1,000+	F.
397	24	20	1-5,000±	1-100:5	1-100+	G.
398	28	10	1-5,000±	1-500:5	....	50%
399	30	25	1-5,000+	1-500:3	1-500+	75%
400	24	10	1-5,000±	1-100:5	1-100+	75%
401	33	16	1-5,000±	1-500:5	1-100+	75%
402	26	8	1-10,000±	1-200:2	1-100+	F.
403	16	2	1-10,000±	1-500:5	....	75%
404	36	6	1-1,000+	1-100:4	....	G.
405	8	22	1-1,000±	1-500:4	....	G.

per cent., was practically free; a third was 75 per cent. benefited, and six patients, or 24 per cent., were 50 per cent. benefited. Following the second successive year's treatment, ten patients, or 40 per cent., were free from symptoms; seven, or 28 per cent., were practically free; seven, or 28 per cent., were 75 per cent. benefited, and one patient, or 4 per cent., was 50

TABLE 6.—PRESEASONAL TESTS AND TREATMENT WITH RAGWEED POLLEN THREE SUCCESSIVE YEARS
(Continued)

G = Good. F = Fair.

Patient	Age of Onset	Duration	Season 1919			
			Tests Before Treatment	Number Treatments with Final Dilution	Tests After Treatment	Result of Treatment
381	38	11	1-1,000 ±	1-500:4	....	F.
382	15	17	1-10,000 ±	1-500:3	....	75%
383	20	10	1-5,000 ±	1-500:5	....	75%
384	32	10	1-10,000 ±	1-500:5	....	F.
385	25	8	1-10,000 ±	1-500:5	....	F.
				Season	1920	
386	9	3	Pol +	1-500:7	....	F.
387	21	5	1-5,000 +	1-500:5	1-500 ±	F.
388	28	15	1-10,000 ±	1-500:4	....	75%
389	..	23	1-1,000 ±	1-500:5	....	F.
390	17	2	1-5,000 ±	1-500:4	....	75%
391	1	34	1-5,000 ±	1-500:5	....	F.
392	20	20	1-5,000 +	1-500:5	1-1,000 +	75%
393	27	5	1-1,000 +	1-500:5	....	75%
394	12	20	1-5,000 ±	1-500:4	1-1,000 +	50%
395	11	39	1-5,000 ±	1-500:6	....	F.
396	21	19	1-1,000 +	1-100:2	....	F.
397	24	20	1-5,000 +	1-500:4	....	75%
398	28	10	1-5,000 ±	1-500:4	....	50%
399	30	25	1-20,000 ±	1-500:5	1-500 +	F.
400	24	10	1-5,000 ±	1-500:5	....	75%
401	33	16	1-5,000 ±	1-100:1	1-100 +	75%
402	26	8	1-5,000 ±	1-100:1	1-500 +	75%
403	16	2	1-10,000 ±	1-100:2	....	G.
404	36	6	1-1,000 +	1-100:4	....	G.
405	8	22	1-500 ±	1-500:6	1-100.0	G.

per cent. benefited. Following the third successive year's treatment, three patients, or 12 per cent., were free from symptoms; ten, or 40 per cent., were practically free; ten, or 40 per cent., were 75 per cent. benefited, and two, or eight per cent., were 50 per cent. benefited. There were no failures in any year. Seven of the twenty-five patients were either entirely free

or practically free from symptoms all three years.

A comparison of the results of the three years' treatments with the amount of treatment given to each patient each year substantiates previous conclusions: (1) Treatment with the 1:100 dilution yielded by far the best results; (2) five or six doses of the 1:500 dilution was followed by excellent results; (3) three or four doses of the 1:500 dilution sometimes was followed by excellent results but more often by 75 per cent. benefit, and (4) two doses of the 1:500 dilution gave poor results.

In twenty-two instances skin tests were done at the end of treatment. Following treatment with the 1:100 dilution of pollen protein, in two instances the 1:100 dilution was negative; in nine instances the 1:100 dilution gave a doubtful to a positive reaction, and in only two instances was the 1:500 dilution at all positive. Following treatment with the 1:500 dilution, in one instance the 1:100 dilution was somewhat positive; in four instances the 1:500 dilution was more or less positive, and in three instances the 1:1,000 dilution was positive. Two of those that were positive with the 1:1,000 dilution were treated four times with the 1:500 dilution, and two of those that were positive with the 1:500 dilution were given only three doses of the 1:500 dilution. Therefore, as shown repeatedly, there is nearly always a great decrease in the sensitivity of the patient, as evidenced by the skin test, following considerable treatment, and

TABLE 7.—PRESEASONAL TESTS AND TREATMENT WITH GRASS POLLENS

THREE SUCCESSIVE SEASONS

G = Good. F = Fair.

Patient	Age of Onset	Duration	Season 1918			
			Tests Before Treatment		Number Treatments with Final Dilution, Timothy	Result of Treatment
			Timothy	Red Top		
410	22	25	1-5,000 ±	1-1,000 +	1-500:3	F.
411	23	10	1-10,000 ±	1-5,000 ±	1-500:5	G.
412	..	..	1-500 ±	1-100 ±	1-500:6	F.
413	15	45	1-1,000 ±	1-100 +	1-100:3	G.

TABLE 7.—PRESEASONAL TESTS AND TREATMENT WITH GRASS POLLENS
THREE SUCCESSIVE SEASONS (Continued)

G = Good. F = Fair.

Patient	Age of Onset	Duration	Season 1919				
			Tests Before Treatment			Number Treatments with Final Dilution, Timothy	Result of Treatment
			Timothy	Red Top	June Grass		
410	22	25	1-5,000 ±	1-5,000 ±	1-1,000 ±	1-100:4	G.
411	23	10	1-10,000 ±	1-5,000 ±	1-1,000 ±	1-100:4	G.
412	..	..	1-500 ±	1-500 ±	1-100 ±	1-100:3	G.
413	15	45	1-500 +	1-500 ±	....	1-100:1	G.

TABLE 7.—PRESEASONAL TESTS AND TREATMENT WITH GRASS POLLENS
THREE SUCCESSIVE SEASONS (Continued)

G = Good. F = Fair.

Patient	Age of Onset	Duration	Season 1920						
			Tests Before Treatment		Number Treatments with Final Dilution			Result of Treatment
			Timothy	Red Top	June Grass	Timothy	June Grass	
410	22	25	1-1,000 ±	1-1,000 ±	1-1,000 ±	1-100:3	1-100:3	50%
411	23	10	1-5,000 ±	1-1,000 +	1-1,000 +	1-100:4	1-500:6	75%
412	..	..	1-100 ±	1-100 ±	1-100.0	1-500:5	1-500:6	G.
413	15	45	1-500 ±	1-500 ±	1-100.0	1-100:2	....	G.

the greatest decrease results from treatment with the 1:100 dilution.

In Table 7 are presented four patients with early hay-fever who were treated three years in succession with the grass pollens. The four patients were either free or practically free from symptoms following treatment with timothy pollen alone the first year, and all were entirely free from symptoms following an increased amount of timothy pollen treatment the second year, even tho two of the patients were equally sensitive to redtop pollen and quite sensitive to June grass pollen. Therefore, as already proven, timothy pollen treatment will protect against redtop pollen and there was no evidence that the patients needed June grass pollen treatment. From the experience of the first two years, there was every reason to believe that similar timothy pollen treatment alone would ensure excellent results the third year. Therefore, it was decided to make an experiment of these four cases by treating three of them with varying amounts of June grass pollen together with sufficient timothy treatment, and to treat the fourth patient with timothy pollen alone as a control. The results were interesting, in that the first patient who had the maximum treatment with both pollen extracts was only 50 per cent. benefited; the second patient who had maximum treatment with timothy pollen, and considerable, tho less, treatment with June grass pollen, was 75 per cent. benefited, whereas the third patient, who had considerable, tho less, treat-

ment with timothy pollen than the other two patients, but who had as much treatment with June grass pollen, was free from symptoms, and the fourth patient, following treatment with timothy pollen extract alone, was also free from symptoms. Therefore, the only difference in the treatment of the first three cases between the first two years and the third year was the additional treatment with June grass pollen in the third year. The greater the amount of treatment with June grass pollen extract, the poorer were the results, and the same number of treatments with June grass pollen in a non-sensitive case and no June grass treatment in a non-sensitive case was followed by excellent results. In order to give the first patient three treatments with the 1:100 dilution of pollen extract, this treatment was carried on in increasing large doses during June grass pollination so that the patient was being treated by and at the same time was being exposed to June grass pollen, and the result was that the patient had much hay-fever during June as a result of treatment with large doses of June grass pollen at the time of natural exposure to the pollen, altho in the previous two years he either was not sufficiently exposed to June grass pollen or he had sufficient protection against it. The second patient was comparable with the first, with the exception that the June grass pollen treatment was discontinued shortly after the onset of June grass pollination, but timothy pollen treatment was continued as in the first case. Therefore,

TABLE 8.—PRESEASONAL TESTS AND TREATMENT WITH RAGWEED POLLEN FOUR SUCCESSIVE YEARS

G = Good. F = Fair. N = None.

Patient	Age of Onset	Duration	Season 1917		
			Tests Before Treatment	Number Treatments with Final Dilution	Result of Treatment
406	5	42	1-1,000 ±	1-100:4	G.
407	31	16	1-1,000 ±	1-100:3	75%
408	21	20	1-5,000 ±	1-100:3	F.
409	15	45	1-5,000 ±	1-500:3	50%

TABLE 8.—PRESEASONAL TESTS AND TREATMENT WITH RAGWEED POLLEN FOUR SUCCESSIVE YEARS (Continued)

G = Good. F = Fair. N = None.

Patient	Age of Onset	Duration	Season 1918		
			Tests Before Treatment	Number Treatments with Final Dilution	Result of Treatment
406	5	42	1-100 ±	1-100:4	75%
407	31	16	1-1,000 ±	1-500:4	F.
408	21	20	1-5,000 ±	1-500:5	50%
409	15	45	1-5,000 ±	1-500:5	F.

the second case had less treatment during June grass pollination and had less symptoms in June so that the result was 75 per cent. benefit. The third patient had as much June grass treatment but was not sensitive to June grass pollen, therefore, June grass treatment during its pollination was harmless and needless as it would have been had it been given to the fourth patient.

The manner in which June grass pollen was

TABLE 8.—PRESEASONAL TESTS AND TREATMENT WITH RAGWEED POLLEN FOUR SUCCESSIVE YEARS
(Continued)

G = Good. F = Fair. N = None.

Patient	Age of Onset	Duration	Season 1919		
			Tests Before Treatment	Number Treatments with Final Dilution	Result of Treatment
406	5	42	1-500 +	1-100:4	75%
407	31	16	1-1,000 ±	1-100:2	G.
408	21	20	1-5,000 ±	1-500:5	75%
409	15	45	1-5,000 ±	1-500:2	N.

TABLE 8.—PRESEASONAL TESTS AND TREATMENT WITH RAGWEED POLLEN FOUR SUCCESSIVE YEARS
(Continued)

G = Good. F = Fair. N = None.

Patient	Age of Onset	Duration	Season 1920		
			Tests Before Treatment	Number Treatments with Final Dilution	Result of Treatment
406	5	42	1-500 ±	1-100:3	75%
407	31	16	1-1,000 +	1-500:4	F.
408	21	20	1-10,000 ±	1-500:6	75%
409	15	45	1-10,000 +	1-500:5	G.

given to the patients in Table 7 differs from the way it was given in the preceding tables in that in these cases treatment with June grass was discontinued before the onset of its pollination, whereas, the patients in Table 7 were treated with gradually increasing amounts of June grass pollen during the time the patients were being naturally exposed to the pollen. Therefore, treatment with large amounts of a pollen ex-

tract during the season of its pollination is evidently not desirable. The conclusion that has already been repeatedly stated, namely, that mixed pollen treatment is, as a rule, not only unnecessary but undesirable, was equally true of cases in Table 7, and the poorer results obtained in the third successive year of treatment was due, as shown repeatedly, to mistreatment.

In Table 8 are presented four patients who were treated with ragweed pollen extract four successive years.

They illustrate the slightly variable results that may be obtained by giving similar treatment each year to the same patient for several years, and by giving varying amounts of treatment to the same patient for several years.

In three of these cases the results exprest on a percentage basis were practically identical for all four years and the only exception to this in the fourth patient was the unfavorable result that followed too little treatment in the third year. In other words, favorable results may be looked for following any number of successive years' treatment, provided the average number of treatments are given each year. No matter how many successive years the same patient is treated, as a rule, approximately the same amount of treatment with the final dilution is required each year as that which gave desirable results any preceding year, however, no greater amount of treatment is required in successive years than that which gave desirable results any preceding year.

During-the-Season or Curative Treatment with Pollen.—Frequently patients present themselves for treatment during their hay-fever attack, and altho pollen treatment at this time does not seem to be very logical, on the basis of anaphylaxis, the patient often will insist on taking the chance. Pollen treatment during the season does not seem logical because the patient is being injected with the pollen which is causing symptoms at the same time that he is being exposed to the pollen present in the air which he is inhaling. The danger resulting from large doses of the injected pollen is obvious because of an overdose, due to the combination of the injected pollen and the inhaled pollen. Therefore, in order that during-the-season treatment should be beneficial, the patient must be injected with minute amounts of the pollen extract in order to diminish artificially a few of the patients antibodies, thus leaving a smaller number of antibodies in the patient for combination with the pollen antigen that is inhaled. If too much pollen extract (antigen) is injected, the patient should have symptoms due to over-treatment alone, or he should be made worse, due to the injection of pollen extract (antigen) superimposed on the inhalation of pollen (antigen). It is evident, that on the basis of anaphylaxis, during-the-season treatment is hazardous, and altho the skin test is the best guide as to the proper treatment, there is no way of controlling the amount of pollen that the patient may inhale.

TABLE 9.—TEST AND TREATMENT DURING SEASON WITH GRASS POLLEN

F = Fair. N = None.

Patient	Previous No.	Tests Before Treatment, Timothy	Dates of Treatment	Treatment in Cubic Centimeters with Dilution of Timothy Pollen	Result of Treatment
			Season 1917		
415	374	1-20,000 ±	6/22 to 7/12	1-20,000 = 0.15, 0.3; 1-10,000 = 0.15, 0.15.....	75%
424	...	1-1,000 ±	6/20 to 6/29	1-1,000 = 0.15; 1-500 = 0.1, 0.15..............	50%
416	...	1-5,000 +	6/22 to 7/14	1-10,000 = 0.15; 1-5,000 = 0.15, 0.3, 0.45; 1-1,000 = 0.15..........................	25%
			Season 1919		
440	...	1-5,000 ±	7/10 to 7/24	1-10,000 = 0.15; 1-5,000 = 0.15, 0.3...........	25%
441	...	1-1,000 +	6/10 to 7/14	1-5,000 = 0.1, 0.15, 0.3, 0.45; 1-1,000 = 0.15, 0.3...	N.
443	...	1-5,000 ±	6/16 to 7/10	1-10,000 = 0.15, 0.3; 1-5,000 = 0.15, 0.3, 0.45..	F.
444	...	1-1,000 +	6/19 to 7/14	1-5,000 = 0.15, 0.3, 0.45; 1-1,000 = 0.15,0.3...	F.
445	208	1-1,000 ±	6/ 5 to 7/ 5	1-5,000 = 0.15, 0.3; 1-1,000 = 0.1, 0.15, 0.3, 0.45...	75%
446	{205 286}	1-1,000 ±	6/16 to 7/14	1-5,000 = 0.15, 0.3, 0.45; 1-1,000 = 0.15, 0.3...	75%
442	...	J. G. 1-500 ±	5/30 to 6/20	J. G. 1-1,000 = 0.15, 0.3; 1-500 = 0.15, 0.3.........	N.

TABLE 9.—TEST AND TREATMENT DURING SEASON WITH GRASS POLLEN (Continued)

F = Fair. N = None.

Patient	Previous No.	Tests Before Treatment, Timothy	Dates of Treatment	Treatment in Cubic Centimeters with Dilution of Timothy Pollen	Result of Treatment
			Season 1920		
452	...	1-10,000±	6/15 to 7/ 6	1-20,000 = 0.15; 1-10,000 = 0.15, 0.3, 0.4......	F.
455	...	1-100+	6/24 to 7/14	1-1,000 = 0.15, 0.3, 0.3, 0.4, 0.45..............	75%
456	...	1-10,000±	6/21 to 7/10	1-20,000 = 0.15; 1-10,000 = 0.15, 0.3, 0.45.....	50%
457	...	1-5,000±	6/26 to 7/17	1-10,000 = 0.15, 0.3; 1-5,000 = 0.15, 0.3, 0.45..	50%
458	...	1-5,000+	6/26 to 7/17	1-20,000 = 0.15; 1-10,000 = 0.15, 0.3, 0.45.....	N.
459	...	1-5,000±	6/24 to 7/17	1-10,000 0.15, 0.3, 0.45, 0.55, 0.65............	F.
460	...	1-5,000±	6/26 to 7/17	1-10,000 = 0.15, 0.3, 0.45, 0.55................	N.
461	...	1-1,000+	6/26 to 7/17	1-5,000 = 0.15, 0.3, 0.45, 0 55.................	25%
462	...	1-5,000±	6/22 to 7/17	1-10,000 = 0.15, 0.3; 1-5,000 = 0.15, 0.3.......	N.
		T. and J. G.		T. and J. G.	
451	...	1-5,000±	6/12 to 7/ 1	1-10,000 = 0.15, 0.3, 0.3, 0.45.................	F.
453	...	1-5,000±	5/29 to 6/22	1-12,000 = 0.15; 1-10,000 = 0.15, 0.3, 0.4......	F.
		J. G.		J. G.	
454	...	1-100+	5/29 to 6/16	1-1,000 = 0.15, 0.3, 0.45......................	F.

In Table 9 are presented twenty-two patients who were treated with grass pollens during the season of their pollination, and while they were having symptoms from exposure to these pollens. Three patients were treated in 1917 with timothy pollen; in 1919, six were treated with timothy, and one was treated with June grass, and in 1920, nine were treated with timothy, two with the combination of timothy and June grass, and one with June grass alone.

Before considering Table 9, it may be well to explain the notations beneath the headings of each column, using the first patient as an example. Four hundred and fifteen is the sequence number of the patient in the whole series presented in this paper. No. 374 in the second column means that this same patient has been presented previously in this paper, and on referring back, it is seen that this patient was presented in Table 5 which consisted of patients who were treated with grass pollen two years in succession; in other words as No. 415 the patient was treated during the season in 1917 (Table 9) and preseasonally two successive years, 1918 and 1919 (Table 5). The third column gives the skin test. The next column gives the dates of treatment, that is June 22 to July 12, inclusive. The treatment column gives the dilutions with which the patient was treated and the respective amounts of each treatment dilution in cubic centimeters; for instance 1:20,000 dilution of timothy pollen extract, dose 0.15 c.c., then 0.3 c.c., after this the 1:10,000 dilution,

dose 0.15 and 0.15 c.c. The five or seven day interval between doses is understood, and usually the same scheme of treatment was followed as outlined in the first part of this paper for preseasonal treatment, and the skin test was used as the guide to determine the initial dose. The last column gives the result from during-the-season treatment, for instance, the first patient was 75 per cent. benefited.

The results from during-the-season treatment were: Of the twenty-two patients treated, none were free from symptoms; seven, or 32 per cent., were practically free; four, or 18+per cent., were 75 per cent. benefited; three, or 13+per cent., were 50 per cent. benefited; the same number were 25 per cent. benefited, and five, or 22+per cent., were not benefited. Since no patients were entirely relieved of symptoms, and since a large percentage were not benefited, it is evident, on comparing these results with those of former tables, that preseasonal treatment ensures better results by far than does during-the-season treatment. If preseasonal treatment is absolutely barred, during-the-season treatment is worth trying, provided it is given with sufficient care and the skin test is used as a guide to the initial treatment.

Patients 442 and 454 were treated with June grass (J. G.) alone because they were sensitive to this pollen only, and were having symptoms during June grass pollination, as noted by the dates of treatment, namely, from the last of May to the middle of June. Patients 451 and

453 were treated with the combination of timothy and June grass pollen extracts because they were having symptoms and were sensitive to June grass, and they were also sensitive to and had had symptoms during the timothy pollination. The other patients were treated with timothy pollen extract alone, because practically all of them were first seen at the end of June grass pollination and at the beginning or during timothy pollination.

With three of the patients we have the opportunity of contrasting during-the-season treatment with preseasonal treatment. Patient 415 was 75 per cent. benefited by during-the-season treatment, and he was similarly benefited by preseasonal treatment in the two following years (Table 5, Patient 374). Patient 445, who was 75 per cent. benefited by during-the-season treatment, was free from symptoms following preseasonal treatment (Table 2, Patient 208). Patient 446, who was 75 per cent. benefited from during-the-season treatment, was similarly benefited following preseasonal treatment (Table 2, Patient 205), and was not benefited following the same amount of preseasonal treatment (Table 3, Patient 286) as was given during the season. It is not advisable to draw general conclusions from these three cases, altho they are of sufficient interest to warrant mention.

In Table 10 are presented twenty-seven patients who were treated with ragweed pollen extract during the season. The notations in this table are exactly like those in Table 9, therefore

TABLE 10.—TEST AND TREATMENT DURING SEASON WITH RAGWEED POLLEN

G = Good. F = Fair. N = None.

Patient	Previous No.	Tests Before Treatment	Dates of Treatment	Treatment in Cubic Centimeters with Dilution of Ragweed Pollen	Result of Treatment
			Season 1917		
417	35a	1-1,000 +	8/14 to 9/28	1-1,000 = 0.15, 0.2, 0.3, 0.4, 0.45, 0.5	75%
418	. . .	1-5,000 ±	9/ 4 to 9/27	1-10,000 = 0.15: 1-5,000 = 0.15; 1-1,000 = 0.15	75%
419	36	1-5,000 ±	8/27 to 9/ 4	1-10,000 = 0.15, 0.3	F.
420	. . .	1-5,000 ±	9/ 6 to 9/24	1-10,000 = 0.15; 1-5,000 = 0.15, 0.3, 0.45	50%
421	. . .	1-1,000 ±	8/10 to 9/ 5	1-5,000 = 0.15; 1-1,000 = .15, .3; 1-500 = 0.15, 0.3, 0.45	25%
422	119	1-10,000 ±	9/ 4 to 9/27	1-10,000 = 0.15, 0.3; 1-5,000 = 0.15, 0.3	N.
423	. . .	1-5,000 ±	8/16 to 9/10	1-10,000 = 0.15, 0.3; 1-5,000 = 0.15, 0.3, 0.45	50%
			Season 1918		
425	371	1-1,000 +	8/17 to 8/29	1-5,000 = 0.15, 0.3, 0.45	N.
426	372	1-1,000 +	8/28 to 9/11	1-5,000 = 0.15, 0.15, 0.2	50%
427	6	1-10,000 ±	8/28 to 9/14	1-20,000 = 0.15; 1-10,000 = 0.15, 0.3	50%
428	59	1-5,000 ±	8/22 to 9/ 5	1-10,000 = 0.15, 0.3, 0.3	50%
429	. . .	1-1,000 +	8/20 to 9/14	1-5,000 = 0.15, 0.3, 0.45; 1-1,000 = 0.15, 0.3	N.
430	. . .	1-1,000 ±	8/16 to 9/ 7	1-5,000 = 0.15, 0.3, 0.45; 1-1,000 = 0.15	50%
431	61	1-1,000 +	8/29 to 9/13	1-5,000 = 0.15, 0.3, 0.45	N.

TABLE 10.—TEST AND TREATMENT DURING SEASON WITH RAGWEED POLLEN (Continued)

G = Good. F = Fair. N = None.

Patient	Previous No.	Tests Before Treatment	Dates of Treatment	Treatment in Cubic Centimeters with Dilution of Ragweed Pollen	Result of Treatment
			Season 1918		
432	346	1-1,000±	8/28 to 9/10	1-5,000 = 0.15, 0.3, 0.45	N.
433	369	1-10,000±	8/13 to 8/30	1-20,000 = 0.15, 0.3; 1-10,000 = 0.15	N.
434	84	1-1,000+	8/28 to 9/10	1-5,000 = 0.15, 0.3, 0.45	N.
435	370	1-1,000+	8/20 to 9/13	1-5,000 = 0.15, 0.3, 0.4, 0.45, 0.5	G.
436	...	1-1,000±	8/16 to 9/24	1-5,000 = 0.15, 0.3, 0.45, 0.45; 1-1,000 = 0.15, 0.3, 0.3	G.
437	...	1-10,000±	8/14 to 9/ 9	1-20,000 = 0.15; 1-10,000 = 0.15, 0.3; 1-5,000 = 0.15, 0.3	N.
438	...	1-5,000±	8/20 to 9/10	1-10,000 = 0.15; 1-5,000 = 0.15, 0.15, 0.3	75%
439	184	1-5,000±	8/14 to 9/14	1-10,000 = 0.15, 0.3; 1-5,000 = 0.15, 0.3, 0.45	N.
447	10	1-10,000+	8/19 to 9/14	1-20,000 = 0.15, 0.3; 1-10,000 = 0.15, 0.3, 0.45	N.
448	...	1-10,000±	9/ 1 to 9/21	1-20,000 = 0.15, 0.3; 1-10,000 = 0.15, 0.3	N.
449	62	1-5,000±	8/29 to 9/11	1-10,000 = 0.15, 0.3; 1-5,000 = 0.15	N.
450	...	1-10,000±	7/31 to 9/21	1-20,000 = 0.15, 0.3, 0.45, 0.55; 1-5,000 = 0.15, 0.3, 0.45, 0.55	50%
463	...	1-1,000+	8/20 to 9/20	1-5,000 = 0.15, 0.3, 0.45; 1-1,000 = 0.15, 0.3	G.

no explanation is needed. It should be stated, however, that these patients were tested with and found to be either not sensitive or only slightly sensitive to other pollens.

Of the twenty-seven patients presented in Table 10, three, or 11 + per cent., were free from symptoms; one patient, or 3 + per cent., was practically free; three patients, or 11 + per cent., were 75 per cent. benefited; seven, or 25 + per cent., were 50 per cent. benefited; one patient, or 3 + per cent., was 25 per cent. benefited, and twelve patients, or 44 + per cent., were not benefited. Therefore, altho a few patients were free from symptoms, and as many more were 75 per cent. benefited, the number who were only 50 per cent. benefited was as great as the number who were more than 50 per cent. benefited, and nearly half of the whole series were not benefited at all. On comparing these results from during-the-season treatment with the results presented in former tables from preseasonal treatment, it is evident that for late hay-fever by far the best results are obtained from preseasonal treatment, and it is questionable whether during-the-season treatment is even worth giving when it is taken into consideration that there are localities to which patients may go where ragweed does not exist.

Since fifteen of these patients have been discust elsewhere in this paper, it is possible with these to compare during-the-season treatment with preseasonal treatment. Ten of the patients were presented in Table 1, therefore

it is possible to contrast the results from the two kinds of treatment in these cases with little detail. Patient 417 (35a) was free from symptoms following preseasonal treatment and 75 per cent. benefited from during-the-season treatment; Patient 419 (36) was free from symptoms following preseasonal and practically free from symptoms from during-the-season treatment; Patient 428 (59) was 50 per cent. benefited as a result of both kinds of treatment; therefore, in these three cases the results from preseasonal treatment were slightly better than those from during-the-season treatment in two of them, and the same in the third case. The other seven cases in this group, namely, Patients 422 (119), 427 (6), 431 (61), 435 (84), 439 (184), 447 (10) and 449 (62) were not benefited by during-the-season treatment, but following preseasonal treatment three were free from symptoms, one was practically free, two were 75 per cent. benefited and the remaining patient was 50 per cent. benefited. Therefore, in these seven cases during-the-season treatment was a failure, whereas preseasonal treatment gave very satisfactory results. Since the remaining five patients in Table 10, that have been presented elsewhere, were all presented in Table 4, they may be considered together with little detail. Patient 426 (372) was 50 per cent. benefited by during-the-season treatment, and was 50 per cent. and 75 per cent., respectively, benefited the two seasons during which he was preseasonally treated; Patient 435 (370) was free

from symptoms from during-the-season treatment and was free from symptoms and 75 per cent. benefited the two respective seasons following preseasonal treatment; therefore, in these two cases, the results from both kinds of treatment were very similar. Patients 425 (371), 432 (346) were not benefited at all by during-the-season treatment, whereas following preseasonal treatment two successive years, Patient 425 (371) was free from symptoms and 75 per cent. benefited, Patient 432 (346) was 75 per cent. benefited both years. Patient 433 (369) was practically free and 75 per cent. benefited. With these three cases, therefore, during-the-season treatment was a failure, whereas preseasonal treatment was very satisfactory.

From these fifteen patients who were treated both ways it may be noted that frequently during-the-season treatment gives as good results as preseasonal treatment. This was true in five, or one-third, of the cases. However, more often during-the-season treatment is a failure in the same cases in which preseasonal treatment is very satisfactory. This was true in ten, or two-thirds, of the cases. These conclusions also verify what was stated in the second preceding paragraph, namely, that for late hay-fever by far the best results are obtained from preseasonal treatment than from during-the-season treatment.

In Table 11 are presented nineteen patients who were treated with bacterial vaccines during their hay-fever attack, altho they were very

sensitive to ragweed pollen and were having hay-fever symptoms during ragweed pollination. The reason for such treatment was that it is quite possible that ragweed pollen exposure may in some cases cause such a severe irritation of the mucous membranes that ever-present bacteria may, either alone or together with ragweed pollen, be a cause of hay-fever symptoms. In our study on pollen asthmatics[8] this was found to be the case in many instances, and Frank and Strouse,[9] Medalia,[10] Scheppegrell[11] and others, have considered this to be true in hay-fever cases. The construction of Table 11 differs from that of Tables 9 and 10 in only two ways, namely, that treatment was given with bacterial vaccines, and that the numerals under the treatment column represent that many hundred millions of bacteria per dose. In some instances, the vaccine used was an autogenous one made from the patient's nasal secretions; in other in-

[8]Walker, I. C.—Sensitization and Treatment of Bronchial Asthmatics with Pollens, Am. J. M. Sc. 157:409, 1919.

[9]Frank, I., and Strouse, S.—Pollen Extracts and Bacterial Vaccines in Hay-Fever, J. A. M. A. 72:1593 (May 31) 1919.

[10]Medalia, L. S.—Hay-Fever; Its Treatment with Autogenous Vaccines and Pollen Extract, Boston M. & S. J. 175:201, 1916.

[11]Scheppegrell, W.—Anaphylaxis Due to Pollen Protein, with a Report of the Results of Treatment in the Hay-Fever Clinic of the New Orleans Charity Hospital, Laryngoscope 28:853, 1919.

TABLE 11.—DURING SEASON TREATMENT WITH BACTERIA

G = Good. F = Fair. N = None.

Patient	Previous No.	Skin Test with Ragweed	Dates of Treatment	Treatment with Vaccines	Each Treatment Recorded in Hundred Million	Result of Treatment
			Season 1919			
464	184 439	1-5,000 ±	8/30 to 9/15	Autog. nasal	3, 4, 5	G.
465	264 181	1-10,000 ±	8/30 to 9/15	Staph. pyog. albus	3, 4, 5	N.
466	...	1-5,000 ±	9/ 6 to 9/14	Autog. nasal	3, 4, 5	50%
467	272	1-5,000 ±	9/10 to 9/24	Autog. nasal	3, 4, 5	75%
468	11	1-10,000 ±	8/23 to 9/13	Staph. pyog. albus	3, 4, 5	N.
469	...	1-10,000 +	9/ 5 to 9/20	Autog. nasal	3, 4, 5	N.
470	185	1-5,000 ±	8/23 to 9/12	Staph. pyog. aureus	3, 4, 5, 6	75%
471	385	1-1,000 +	8/29 to 9/18	Autog. nasal and alb	3, 4, 5, 6	N.
472	187	1-10,000 ±	8/20 to 9/18	Autog. strept	3, 4, 5, 6	G.
			Season 1920			
473	463	1-1,000 +	9/ 4 to 9/20	Mixed strept	3, 4, 5	N.
474	...	1-5,000 +	8/30 to 9/20	Mixed strept	3, 4, 5	50%
475	...	1-1,000 +	9/ 6 to 9/20	Mixed strept	3, 4, 5	N.
476	10	1-10,000 +	8/23 to 9/20	Mixed strept	3, 4, 5, 6, 7	N.
477	...	1-5,000 ±	8/23 to 9/13	Mixed strept	3, 4, 5, 6	25%
478	...	1-500 +	8/30 to 9/20	Mixed strept	3, 4, 5, 6	50%
479	...	1-1,000 +	9/ 4 to 9/20	Mixed strept	3, 4, 5	N.
480	186	1-10,000 ±	8/30 to 9/20	Mixed strept	3, 4, 5, 6	F.
481	102	1-5,000 ±	9/ 4 to 9/11	Mixed strept	3, 4	50%
482	154	1-5,000 +	9/ 4 to 9/11	Mixed strept	3, 4	F.

stances it was a stock vaccine consisting of *Staphylococcus pyogenous aureus or S. albus;* and, for those patients who were treated in 1920, a mixed streptococcus vaccine was used. This mixed streptococcus vaccine consisted of equal amounts of the six streptococci that were most frequently found in the sputum and nasal secretions of asthmatic patients.[12] These streptococci, according to Holman's classification, were hemolytic types *S. pyogenes, S. infrequens* and *S. anginosus* and non-hemolytic types *S. salivarius, S. ignavus* and *S. mitis* in the proportion of approximately sixteen million of each per one hundred million of total, so that a dose of 300 million mixed streptococci represented about fifty millions of each of the six strains.

Since Patients 466, 469, 474, 475, 477, 478 and 479 had not been previously observed or treated by me, their cases will be considered together and not too much stress will be placed on the results. Patient 466 was 50 per cent. benefited and Patient 469 was not benefited by treatment with autogenous vaccines made from the nasal secretions. Patients 474 and 478 were 50 per cent. benefited, and Patient 477 was 25 per cent. benefited by the mixed streptococcus vaccine. Patients 475 and 479 were not benefited by the mixed streptococcus vaccine. The only conclusion to be drawn from these cases

[12]Walker, I. C., and Adkinson, J.—Types of Streptococci Found in the Sputum of Bronchial Asthmatics, J. M. Research 40:229, 1919.

is that sometimes an autogenous nasal vaccine or a mixed streptococcus vaccine given during the hay-fever attack benefits somewhat an occasional patient but just as often this treatment fails.

The twelve following patients, however, since they were treated with ragweed pollen either during or preceding the ragweed season in some year, give more definite information. Patients 464 (184 and 439) and 472 (187) were relieved of symptoms while being treated with their autogenous nasal secretion vaccine, whereas both patients were only 50 per cent. benefited from preseasonal pollen treatment (Table 1, Patients 184 and 187) and one patient was not benefited at all by during-the-season pollen treatment (Table 10, Patient 439). In these two control cases it may be assumed that bacteria played some part, at least, in the cause of symptoms. Since Patients 468 (11), 471 (385), 473 (463) and 476 (10) were not benefited by vaccine treatment but all had been free from symptoms from ragweed pollen treatment, it is certain that bacteria played no part in the causation of their hay-fever symptoms. These four patients had been treated with ragweed pollen extract: Patients 468 (11) and 476 (10), preseasonal one year and were free from symptoms (Table 1, Nos. 10 and 11); Patients 471 (385), preseasonal three years in succession and was free from symptoms two years and practically free the third year (Table 6, No. 385); Patient 473 (463) treated during the season was free from symp-

toms (Table 10, No. 462). Patient 465 who was not benefited by either *Staphylococcus pyogenes albus* vaccine or by too little preseasonal treatment (Table 3, No. 264), and was only 50 per cent. benefited by considerable preseasonal treatment (Table 1, No. 181) gives no information with the exception that *Staphylococcus pyogenes albus* played no part in the causation of hay-fever symptoms in this case; this same organism was used in two cases already discust, Patients 468 and 471, with no benefit. Patients 480 (186) and 482 (154) both became practically free from symptoms during mixed streptococcus vaccine treatment, whereas from preseasonal pollen treatment both were benefited only 75 per cent. (Table 1, Nos. 186 and 154); therefore, in these two cases streptococci probably played a considerable part in the causation of hay-fever symptoms. Patient 470 (185) was 75 per cent. benefited during treatment with *Staphylococcus pyogenes aureus* vaccine, whereas only a 50 per cent. benefit followed preseasonal pollen treatment (Table 1, No. 185), therefore *Staphylococcus pyogenes aureus* probably played some part in the causation of hay-fever symptoms in this case. Patient 481 (108) was 50 per cent. benefited during mixed streptococcus vaccine treatment, but was not improved by preseasonal pollen treatment (Table 1, No. 108); therefore, in this case it is quite evident that streptococci played a part in the causation of hay-fever symptoms.

The series of patients who were treated with

bacterial vaccines is too small to justify sweeping conclusions, however, it does seem as tho treatment with bacterial vaccines were beneficial for a few hay-fever patients who are very sensitive to pollen. If a vaccine is to be used, the choice of bacteria would seem to be either an autogenous nasal or a mixed streptococcus vaccine. In the few cases in which considerable preseasonal pollen treatment is not very satisfactory, it is worth while to try during-the-season treatment with autogenous nasal secretion or a mixed streptococcus vaccine.

In Table 12 are presented eighteen patients who were treated with ragweed pollen both preceding and during the season. The first nine patients were given the usual preseasonal pollen treatment and then this treatment was discontinued. A little later, during the same season, these patients reported that they were having more or less hay-fever so that during-the-season treatment with pollens was then given as described in Table 10; in other words, the two methods of treatment were given to these patients. The other nine patients were treated with gradually increasing doses of the pollen extract, but the treatment was begun so late preseasonally that not enough treatment would have been given had treatment been discontinued at the onset of pollination; therefore, the usual preseasonal treatment, using gradually increasing doses, was continued on through the season of pollination. For example, Patient 492 was treated with gradually increasing amounts of

TABLE 12.—PRECEDING AND DURING SEASON TREATMENT WITH RAGWEED POLLEN

S = Same. N = None. W = Worse. F = Fair.

Patient	Previous No.	Tests Before Treatment	Dates of Treatment	Treatment in Cubic Centimeters with Dilution of Ragweed Pollen	Result of Treatment
483	14	1-1,000 ±	8/21 to 9/10	1-5,000 = 0.15, 0.3, 0.45, 0.55	50%
484	308	1-1,000 ±	8/23 to 9/10	1-5,000 = 0.15, 0.3, 0.45	S.
485	18	1-5,000 ±	8/22 to 9/ 3	1-5,000 = 0.1, 0.2, 0.3	S.
486	314	1-5,000 ±	8/21 to 9/10	1-10,000 = 0.15, 0.25; 1-5,000 = 0.15, 0.25	N.
487	399	1-10,000 ±	8/26 to 9/10	1-10,000 = 0.15; 1-5,000 = 0.1, 0.2	W.
488	317	1-1,000 ±	8/20 to 9/ 3	1-1,000 = 0.15; 1-500 = 0.15, 0.15	S.
489	33	1-5,000 +	8/22 to 9/18	1-10,000 = 0.15, 0.25, 0.35; 1-5,000 = 0.2, 0.2	50%
490	320	1-5,000 ±	8/28 to 9/10	1-10,000 = 0.15, 0.25, 0.35	N.
491	35	1-5,000 ±	8/21 to 9/10	1-5,000 = 0.15, 0.25, 0.35	S.
492	...	1-5,000 ±	7/18 to 9/10	Usual treatment including 1-500 = 0.55	N.
493	...	1-10,000 ±	7/ 7 to 9/20	Usual treatment including 1-500 = 0.55	50%
494	...	1-20,000 ±	6/30 to 9/13	Usual treatment including 1-500 = 0.65	75%
495	...	1-10,000 ±	6/14 to 9/ 4	Usual treatment including 1-500 = 0.25	75%
496	...	1-5,000 ±	7/ 3 to 9/13	Usual treatment including 1-500 = 0.25	75%
497	469	1-5,000 +	7/10 to 9/20	Usual treatment including 1-500 = 0.25	50%
498	...	1-10,000 ±	7/ 3 to 9/ 4	Usual treatment including 1-500 = 0.45	F.
499	...	1-5,000 ±	7/ 3 to 9/ 4	Usual treatment including 1-500 = 0.3	50%
500	...	1-10,000 ±	7/10 to 9/20	Usual treatment including 1-500 = 0.25	50%

ragweed pollen extract from July 18 to September 10 inclusive; the usual preseasonal treatment was begun preseasonally and continued into or through the season of pollination.

Patients 483 and 489 were not benefited by preseasonal treatment (Table 1, Nos. 14 and 33); they were then given during-the-season treatment, as indicated in Table 12, with the result that they were 50 per cent. benefited. Patients 485 and 491 were benefited 75 and 50 per cent., respectively, following preseasonal treatment (Table 1, Nos. 18 and 35); they were then given during-the-season treatment, as indicated in Table 12, with no apparent change in their symptoms. Patients 484, 486, 488 and 490 were all unimproved by during-the-season treatment following the preseasonal treatment (as indicated in Table 4, Nos. 308, 314, 317 and 320) which in two cases failed to benefit and in the two others there was a 50 per cent. benefit. The remaining patient (487 was not as much benefited while being treated during the season as he had been by preseasonal treatment) (Table 6, No. 399). Therefore, in only two of these nine cases did during-the-season treatment improve the results already obtained from preseasonal treatment, but since these two patients were not benefited by preseasonal treatment (Table 1, Nos. 14 and 33) and became 50 per cent. benefited by during-the-season treatment, the latter treatment was worth trying after the former had failed; in other words, two failures were changed to 50 per cent. benefit.

The remaining nine patients were treated according to the pre-season schedule, but treatment was begun very late (in July) and continued into the hay-fever season. Altho this is the first time this method of pollen treatment has been mentioned in this paper, it has been used extensively in the past by many investigators. The results from this method of treatment, as indicated in Table 12, show that no patients were entirely free from symptoms; one patient, or 11 per cent., was practically free; one-third of the patients were 75 per cent. benefited; 44 per cent. were 50 per cent. benefited, and one patient, or 11 per cent., was not benefited. Of course, this series of cases is much too small to warrant conclusions, yet it would seem fair to say that this method of treatment is preferable to during-the-season treatment alone but not as desirable as the regular preseasonal treatment which is begun early enough to permit of its discontinuance just prior to the season of pollination.

Hay-Fever Caused By the Pollen of Trees.—So far in this paper we have been concerned with the two pollen seasons, namely, August and September (ragweed) and May to August (the grasses). There is a third and earlier pollen season which begins in March and continues into June, during which time various trees pollinate. Silver maple often pollinates in February; the other maples, birches, willows and hazel nut pollinate in late March or early April; the poplars, juniper, cottonwood and elm polli-

nate during April; the oaks, ash, bayberry and hickory pollinate during May; the pines pollinate in late May and early June, and the fruit trees pollinate in May. I have observed twelve patients who were sensitive to and had hay-fever from the pollen of trees. One patient had hay-fever caused by the pollen of apple-blossoms, and he was free from symptoms following preseasonal treatment with its pollen extract. One patient, who was sensitive to the pollen of the oak and maple, and another, who was sensitive to the pollen of the willow, were both free from symptoms following preseasonal treatment with these pollen extracts. Patients not treated were those sensitive to the following tree pollens; one patient, to poplar tree pollen; one, to pine tree pollen; two, to ash; one, to willow; two, to both willow and poplar, and one to willow, poplar and ash. Since the season of pollination of the individual trees continues only from a few days to two weeks at the most, it does not seem essential that treatment be given.

Other Pollens that May Cause Hay-Fever.— It has been shown in this paper that the chief causes of hay-fever occurring in the New England States were the pollens of ragweed, timothy and June grass; that an occasional cause is the pollen of the rose and redtop grass and of various trees. There is, however, almost an unlimited list of pollens that may at any time, but probably rarely, cause hay-fever. Therefore, for those who treat a large number of hay-fever patients and for those who fail to obtain satis-

factory results from treatment with the common pollens mentioned, it is advisable to have a very extensive assortment of pollens. As a rule, however, it would seem to be sufficient to warn the ragweed patients that they should not smell of goldenrod, golden-glow, sunflower, poppy, aster, chrysanthemum and the like that pollinate during the ragweed season. The grass cases may be warned to avoid close contact with clover, lilies, daisy, dandelion, rose, lawn grass, orchard grass, corn and the like that pollinate during the grass season. In certain localities in this country it may be necessary to treat with the pollen extracts of the various grains, with sunflower or what not, but this necessity is not universal and is limited to the various localities where exposure to these particular pollens is unavoidable.

Other Parts of Plants that May Cause Hay-Fever.—The leaves of certain plants and trees may cause hay-fever. The under surface of some leaves has a fine hairy growth, and these fine hairs may cause hay-fever. I have observed one patient who had hay-fever from and was sensitive to the hairs of the willow tree leaf; treatment with an extract of these leaves prevented hay-fever. Another patient was sensitized to and had hay-fever from the plantain leaf. It is quite probable that the plane tree, the common shade tree in London, may cause hay-fever. Such instances, however, are extremely rare and need not be considered, as a rule.

Foods May Cause Seasonal Hay-Fever.—Seasonal hay-fever, due primarily to foods, has not

come to my notice. However, during their season many hay-fever patients find that certain foods aggravate their symptoms, whereas these same foods may be eaten without symptoms at a time when they are not accustomed to have hay-fever, and they can eat the foods during their hay-fever season, provided they have had sufficient pollen treatment to protect them against the particular pollen that primarily causes their hay-fever. These foods are usually the fruits, and they have no apparent relationship to the causative pollen. Among the usual fruits should be mentioned peach, melon and apple. Green corn and the use of beer and wine often aggravate ragweed hay-fever, but they do not aggravate grass pollen hay-fever as one would expect to be the case; celery sometimes acts similarly. With the peach it is often the skin that causes trouble, whereas the pulp usually does not. The cooking of the fruits often renders them inert.

Animal Emanations May Cause Seasonal Hay-Fever.—The patient who is sensitive to animal emanations usually has symptoms on exposure to the animal at any and all times of the year; occasionally, however, such a patient has symptomps only from exposure to the animal during the spring and summer, when the animal is shedding, moulting or perspiring profusely.

Bacteria May Cause Seasonal Hay-Fever.—The possibility of bacterial infection as a complication of or secondary to pollen sensitization has already been discust, and the possibility

of bacterial infection as a primary cause of hay-fever in patients who are not sensitive to pollens must be considered. Each year I examine three or four patients who have seasonal hay-fever, but who are not sensitive to any of the pollens; therefore, these patients are treated with their autogenous nasal secretion vaccine.

REPORT OF CASES

Case 1.—L. W., a woman, aged 35, has had hay-fever from August first to the end of October for three years. Her symptoms are sneezing, running of the nose and some wheezing.

Not only were the skin tests with pollens negative, but she also failed to give an ophthalmic test, and snuffing the whole pollen of ragweed and dropping a concentrated solution of ragweed pollen extract into her nose failed to provoke symptoms.

The patient was treated with an autogenous vaccine, made from her nasal secretion, in gradually increasing amounts, beginning with 300 million streptococci, from June 25 to Oct. 11, 1919. At the end of the season, she reported that in previous summers she had always lost three weeks of sleep, whereas during the past summer she had lost only one week of sleep, and that her days had been quite free from symptoms.

In June, 1920, she reported that her hay-fever had begun about three weeks previously. She was again treated as previously, from June 7

to July 12, when she discontinued treatment because she had been entirely free from symptoms for the past three weeks and she continued to be free during the summer.

CASE 2.—H. S. M., a woman, aged 29, has had hay-fever for five years, from August 15 to the first frost. The symptoms are sneezing, tickling in the throat and running of the nose, alternating with stuffing up of the nose. She was first seen in June, 1918, and her symptoms had already begun this year, much earlier than usual.

She was treated with gradually increasing amounts of an autogenous vaccine made from her nasal secretion, from June 21 to August 14; the first treatment was 300 million streptococci. In the winter following this treatment, she reported that she had had only six bad days of hay-fever during the whole summer; she claimed that she had been markedly free from hay-fever.

The patient returned the following year, in May, 1919, and reported that her sneezing and running of the nose had just begun again. She was treated again with a new autogenous vaccine in a similar manner as was done the preceding year. During the first six weeks of treatment, she had occasional attacks of hay-fever, but not as bad as usual, during the remainder of the summer she was practically free from hay-fever.

CASE 3.—E. L. T., a woman, aged 30, has had hay-fever for four years, from August to the first frost. Her hay-fever is worse at night and prevents sleep. Her present attack began August 26. She was not sensitive to pollens.

She was treated from September 1 to October 6, inclusive, with an autogenous nasal secretion vaccine consisting of *Staphylococcus pyogenes aureus* in gradually increasing amounts, beginning with 300 million bacteria; during the season, she was given treatment with vaccines. Following the first treatment, she was a little better, and following each succeeding treatment she was free from symptoms for four days but had considerable hay-fever the two days preceding each treatment.

These three patients would seem to prove that there are cases of seasonal hay-fever not caused by pollens but caused by bacteria and that treatment with autogenous vaccines made from their nasal secretions is often very effective. It is noted that in these non-sensitive pollen cases of hay-fever there was an absence of eye symptoms, as noted in a previous paper.[13]

Hay-Fever Caused by Olfactory Irritants or Pseudo-Hay-Fever.—Goodale[14] called attention to the fact that during pollen seasons certain individuals who are sensitive to and have hay-fever from pollens also have vasomotor symptoms ranging from sneezing to asthmatic attacks due to the fragrance of certain heavily scented flowers that have no pollen or to which pollen the

[13] Walker, I. C.: Frequent Causes and the Treatment of Perennial Hay-Fever, J. A. M. A. 75: 782 (Sept. 18) 1920.

[14] Goodale, J. L.: The Present Status of Immunization in Hay-Fever. Boston M. & S. J. 179:293, 1918.

individual is not sensitive. He considers that the symptoms are reflex and that the path of transmission is along the olfactory nerve. The flowers most commonly responsible are lilies, hyacinths, sweet peas, lilacs, honeysuckle and peonies.

I classify the causes of symptoms as mechanical, chemical, odorific and thermal. Among the mechanical causes any kind of dust is the most frequent cause, more especially sweeping dust and hay dust; fine powder, such as talcum and the like, is also a frequent cause. Among the chemical irritants, soap powder, lye and ammoniacal fumes are very frequent causes. Among the odorific irritants, heavily scented perfumes, face powders, musty air and stable odors are frequent causes. Thermal irritants concern sudden changes of temperature, as in going from warm air to extreme cold, from moist air to very dry air, and exposure to drafts; a very frequent history is that of a paroxysm of sneezing with or without running of the nose on retiring and arising. The mechanism seems to be a reflex due to the sudden exposure of the warm and protected skin of the body to cold air, as in getting out of bed and in undressing, during which acts the warm body surface is suddenly and momentarily exposed to cool air; in other words, there is a mild chilling of the body surface.[15] The same mechanism holds for many who take cold easily. Appropriate pollen

[15] Mudd, S., and Grant, S. B.: Reactions to Chilling of the Body Surface, J. M. Research 40:53, 1919.

TABLE 13.—PRESEASONAL TREATMENT WITH RAGWEED POLLEN EXTRACT

G = Good. F = Fair. N = None.

1917		1918		1919		1920		Total		Results
Number of Patients	Percentage of Total Patients	Number of Patients	Percentage of Total Patients	Number of Patients	Percentage of Total Patients	Number of Patients	Percentage of Total Patients	Number of Patients	Percentage of Total Patients	
19	70	26	32	52	37	13	7	110	25	..........G
1	4	9	11	32	23	48	25	90	20	..........F
4	15	23	28	31	22	82	43	140	32	.......75%
3	11	16	20	15	10	45	23	79	18	.......50%
0	0	7	8½	10	7	3	1½	20	4½	..........N
27	..	81	..	140	..	191	..	439	..	......Total
B. Preseasonal Treatment with Grass Pollens										
8	80	10	66	13	72	5	14	36	46	..........G
0	0	3	20	1	5	7	20	11	14	..........F
1	10	2	13	2	11	12	33	17	21.8	.......75%
1	10	0	0	2	11	8	23	11	14	50
0	0	0	0	0	0	3	8½	3	4	..........N
10	..	15	..	18	..	35	..	78	..	......Total

treatment for those who are sensitive usually relieves these symptoms.

SUMMARY

The methods used by me in testing and treating seasonal hay-fever and the seasons of pollination of the causative pollens are described in detail. Eight tables are then presented to illustrate the benefits obtained by preseasonal pollen treatment. Table 3 shows the unsatisfactory results obtained by giving less than three doses of the 1:500 dilution of the pollen extract, and the other seven tables show the good results obtained when more than three doses of the 1:500 dilution, or preferably one or more treatments with the 1:100 dilution of the pollen extract are given. Tables 1 and 2 deal with a single season's treatment, and Tables 4 to 8 inclusive, deal with two or more successive seasons' treatment. In general, the greater the amount of treatment given, the better the symptomatic results and the greater is the reduction in the positiveness of the skin test. Table 13 is a composite of Tables 1 to 8 inclusive, with the exception of Table 3 which concerns insufficient treatment. It shows the results obtained from preseasonal treatment with ragweed pollen and with the grass pollens for each year and the results for all four years.

The percentage of results varies somewhat for different years; this is due, in great part, to variation in treatment. The average results

for all four years following preseasonal ragweed treatment show that nearly 50 per cent. of the patients had little or no symptoms, and a third of the others were 75 per cent. benefited; whereas in only 4.5 per cent. of all of the cases was there failure from treatment. In some of the individual years, treatment showed much better results than this. The average results of treatment with the grass pollen group of cases shows that 60 per cent. of the patients had little or no symptoms, and 21.8 per cent. were 75 per cent. benefited, whereas 4 per cent. were not benefited. In some of the individual years, treatment gave much better results than in other years, and this variation was due to varying treatment. Unless patients return for future treatment, it is very difficult to get in touch with them in order to find out the permanency of relief from treatment. In four cases, however, it has been possible to learn that more or less permanency of benefit follows sufficient preseasonal treatment. Case 11, treated in 1917, was also free from symptoms in 1918 and 1919 without any treatment, but in 1920 this patient had severe symptoms. Case 1 was free from symptoms following treatment but has not been heard from since. Case 70 was free from symptoms following treatment in 1919, and was also free from symptoms in 1920, without treatment. Case 312, free from symptoms in 1918 and 1919 following treatment both years, had no symptoms in 1920 without treatment.

Tables 9 and 10 deal with during-the-season

pollen treatment, and the general conclusion is that during-the-season pollen treatment with the grasses is worth doing but is not as satisfactory as the preseasonal treatment, and that during-the-season treatment with ragweed pollen is very unsatisfactory. Treatment for the early type of hay-fever seems to yield better results than treatment for the late type. This is probably due to the fact that there are several causes for the early type of hay-fever such as June grass, rose and timothy pollen all of which pollinate at different times and each over a short interval and it is usually only one of these pollens that cause symptoms. Therefore, the actual cause of early hay-fever is present a short time, whereas ragweed which is practically always the only cause of late hay-fever pollinates as long a time as all of the early pollens together, and a much longer time than any one of the early pollens.

Table 11 presents pollen sensitive patients who were treated with bacterial vaccines, and there is evidence that bacteria may, in some pollen sensitive cases, play a part in the cause of hay-fever symptoms. With those patients who are not sufficiently benefited by supposedly satisfactory preseasonal pollen treatment, treatment with autogenous nasal vaccines is indicated during the pollen season.

Table 12 presents cases treated with ragweed pollen preceding and during the season. In the case of patients not much benefited by satisfactory preseasonal pollen treatment, small doses of the pollen protein given during the season

may produce benefit. In the case of those patients who present themselves too late for sufficient preseasonal treatment, gradually increasing amounts of the pollen protein may be given throughout the hay-fever season. The results from this kind of treatment seem to be better than those from during-the-season treatment alone with either pollens or bacteria but not nearly as satisfactory as the result obtained from preseasonal pollen treatment that is begun early enough to permit of its discontinuance before the season of pollination.

Since close contact with pollens that are closely related to the causative pollen, the eating of fruits, and certain olfactory irritants may all complicate the cause and the treatment of hay-fever, it is not remarkable that hay-fever treatment does not always afford entire protection.

Other causes of seasonal hay-fever that must be considered are tree pollens, animal emanation and bacteria.

CONCLUSIONS

Satisfactory preseasonal pollen treatment yields excellent results in seasonal hay-fever. By satisfactory treatment is meant five or six treatments with a 1:500 dilution of the pollen extract, or, better still, two or three treatments with a 1:100 dilution of the pollen extract.

When preseasonal pollen treatment fails, sometimes benefit results from during-the-season treatment with pollens and sometimes from during-the-season treatment with an autogenous

nasal secretion vaccine. During-the-season treatment with pollens without preseasonal treatment is not very satisfactory altho such treatment for the early type of hay-fever is worth doing provided for some reason or other it is not possible to give preseasonal treatment.

Treatment that of necessity must begin late preseasonally may be continued on through the pollen season with better results than those obtained by during-the-season treatment alone, but with much less beneficial results than those obtained by beginning preseasonal treatment early enough to permit of its discontinuance before the season of pollination begins.

Altho in the New England States the pollen of ragweed (dwarf variety) is practically always the cause of late hay-fever (August and September), and the pollen of timothy grass is the cause of probably 90 per cent. of the early hay-fever (June and July), in other localities other pollens may play a great part in the cause of either type of hay-fever. For this reason it is essential that other observers publish their tests, results and treatment in detail in order to learn the causative pollens and proper treatment in various localities.

In the New England States the pollen of rose and redtop grass occasionally cause early hay-fever, and treatment occasionally has to be given with these. The pollen of June grass is a more or less common cause of early hay-fever but when the season of its pollination is very early, unless the treatment is begun very early,

too little treatment can be given with it to be of benefit, and when its pollination is very late, sufficient treatment with timothy pollen has been given to protect against June grass pollen exposure.

Treatment with a combination of timothy and June grass pollens was not successful in my hands because of insufficient treatment with both pollens; the addition of June grass pollen retarded the amount of treatment that otherwise would have been given with timothy alone. Another illustration of the undesirability of mixed pollen treatment is noted with those patients who have both the early and the late types of hay-fever. In these cases, during the month of May and part of June, large amounts of timothy pollen extract should be given together with small amounts of ragweed pollen extract, and the result in these cases is rather poor because there is a tendency to restrict the timothy treatment for fear of producing anaphylaxis from the combination of two pollens to which the patient is sensitive. In other words, treatment with a combination of pollens either diminishes the amount of treatment that is required with one or all of them or pushing the treatment with the combination leads to the danger of anaphylaxis. For either or both of these reasons, I see no benefit to be derived from mixed pollen therapy. As regards the early type of hay-fever, I consider it best to treat preseasonally with timothy or the chief causative pollen and, if necessary to treat during the season with June grass pollen.

Since intimate exposure to other pollens which may be attributing causes of hay-fever, the eating of fruits during the hay-fever season, the possibility that bacteria play a part in the cause of hay-fever and the exposure to olfactory irritants may all aggravate the symptoms of hay-fever, it is not remarkable that hay-fever treatment is not perfect.[16]

16. Selfridge,[17] Koessler[18] and Scheppegrell[19] have published the prevailing pollens in their respective localities, namely, California, Illinois and the Southern States and they designated those pollens that seem to be the chief causes of hay-fever in these localities. It is desirable that others in various localities do likewise.

17. Selfridge, G.: Spasmodic Vasomotor Disturbances of the Respiratory Tract, with Special Reference to Hay-Fever, California State J. M. 16: 164, 1918.

18. Koessler, K. K.: The Specific Treatment of Hay-Fever (Pollen Disease), Billings-Forchheimer Therapeusis of Internal Diseases, 5: New York, D. Appleton & Co.

19. Scheppegrell, W.: Hay-Fever in the Southern States, Southern M. J. 9: 614, 1916.

7. The Present-Day Conception of Hay-Fever*

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It is hardly necessary to define the term "hay-fever" since the disease is so common that every one is quite familiar with the symptom-complex with which this term is associated. Nevertheless, there are so many other conditions in which this group of symptoms is predominant that it may be wise to restrict the term to those cases in which the etiological factor is the pollen of one or more plants. Barker[1] defines the disease as "a more or less severe inflammation of the mucous membranes of the nose, throat and bronchi, occurring in susceptible persons in the spring or in the autumn and caused by the inhalation of pollens of certain plants."

Historical.—It was not until 1873 that Blackley,[2] as a result of careful researches, called attention to the periodicity of the disease, and definitely established the relationship existing

*From the Department of Medicine, University of Toronto. Courtesy of the Canadian Medical Association Journal. Read before the Hastings County Medical Society, October 13th, 1920.

[1]Barker.—"Monographic Medicine," vol. 2, 1916.
[2]Blackley.—*British Med. Journ.*, 1898, 1, 867.

between the attacks and the presence of certain pollens in the air at these periods. In 1905 Dunbar[3] confirmed Blackley's observations and extended them. He introduced the method of treatment by the use of pollen, but believed that his extract of pollen was a true toxin which, upon inoculation into horses would call forth the production of antitoxin. This immune serum he called Pollantin, and used it in an attempt to produce a passive immunity in the patient. The results have not been sufficiently favorable to warrant the adoption of the method.

Since then, many investigators have devoted long and careful study to this disease and *active* prophylactic immunization by means of pollen extracts has definitely been established as the best method of treatment at our command.

Protein Sensitization.—In individuals who manifest a hypersusceptibility to a protein, the administration of such protein, either hypodermically or intravenously, gives rise to a more or less violent reaction which may manifest itself by symptoms of profound shock, an attack of asthma, or the symptom-complex of hay-fever. Sometimes these symptoms may be brought on by the mere ingestion of the offending protein, or by its absorption through the mucous membranes of the nasal passages and bronchi. It has long been held by many observers that these phenomena are of the nature of anaphylaxis. More recently, observations on drug hypersus-

[3] Dunbar.—*Berliner klin. Woch.*, 1905, 11, 635.

ceptibility in which there is no protein element, have cast some doubt upon the adequacy of this explanation. The writer had occasion to test a patient (a physician) in Walker's clinic, complaining of asthma and eczema, in whom the attacks were brought on while administering arsphenamine. Cutaneous tests with a solution of this drug yielded a result comparable in every way to those obtained in cases sensitive to proteins. Quinin has also been found to produce a similar result in suitable cases. Coca[4] urges that the term anaphylaxis be restricted to instances where the result is shown to be due to an antigen-antibody reaction, and claims that a true case of anaphylaxis in a human being has never yet been reported. He suggests the term "allergy" to cover all instances in which there is no proof of an antigen-antibody reaction. The term is by no means a new one but his suggested restriction of its use is new. A full discussion of this question is not within the scope of the present paper and it will be necessary to content ourselves with the statement that while the majority of investigators still favor the anaphylaxis theory to explain the phenomena of hay-fever and bronchial asthma, there are serious objections which will have to be satisfactorily dealt with before the question is finally settled.

The table on following page taken from Walker,[5] is an excellent means of visualizing the

[4]Coca.—"Tice's Practice of Medicine," vol. 1, W. F. Prior Co., 1920.

[5]Walker.—"Oxford Medicine," 1920, vol. 2.

CLASSIFICATION OF HAY-FEVER (WALKER)

- Sensitive Cases
  - Seasonal
    1. tree protein
    2. grass protein
    3. compositæ protein
    4. Animal hair protein
    5. bacterial protein
    6. food protein
  - All the year
    1. animal hair protein
    2. bacterial protein
    3. food protein
- Non-sensitive Cases
  - Seasonal
    1. bacterial infection
  - All the year
    1. bacterial infection
    2. abnormalities of nasal passages and sinuses

various causes of hay-fever and their relationships to each other. The non-sensitive cases are nearly always due to bacterial infection and should not properly be called hay-fever. These cases are characterized by a more tenacious type of secretion rather than the typical thin, watery discharge of true hay-fever. Moreover, the eyes are less commonly affected and the whole picture more closely resembles an ordinary coryza, or common "cold." It is not difficult to conceive of such a phenomenon occurring during certain seasons of the year,—particularly in the autumn and winter. It may also be present more or less continuously throughout the year. Cases of so-called spasmodic vasomotor rhinitis occurring as a result of the presence of abnormalities of the nasal passages and sinuses are comparatively uncommon, and as Barker suggests, "the physician should protect the hay-fever patient from the useless nasal operations of over-zealous surgical enthusiasts!" There are, nevertheless, certain cases presenting symptoms *simulating* non-seasonal hay-fever, which are relieved after the removal of polyps or other gross abnormalities.

Seasonal Sensitive Cases.—During April and May the various trees pollinate,—each variety requiring approximately two weeks or less to complete the process. Therefore, if an individual is sensitive to willow, for example, the attack will last only a very short time and specific treatment will not be worth while. If, however, the patient is sensitive to a number of pollens which are shed at different times, the attack

may last for a considerable period, and prophylactic inoculation may be advisable. Such cases are comparatively rare.

The next pollen season begins in early June and lasts until the latter part of July. During this time the grasses shed their pollens. It is true that other pollens are also met with in this period, for example, that of the rose and of the daisy, but these seldom cause hay-fever, in spite of the popular belief as evidenced by the familiar terms "rose cold" or "rose fever." The chief cause of the disease during this season is the pollen of timothy, with that of June grass and redtop ranking next. The term "hay-fever" in its narrow sense should really be restricted to the cases occurring during this period,—since it is only at this time that the pollens of grasses used in making hay are the causative agents.

The third and most important pollen season begins in this country about the twentieth of August,—often a few days earlier. It lasts until the first heavy frost, which usually occurs the first week in October. During this season the chief offender is the pollen of ragweed. Occasionally goldenrod and daisy are found to be causal agents. It is true that very often in testing the patients for sensitiveness all three pollens are found to yield a positive result, but almost invariably that of ragweed causes by far the strongest reaction, with goldenrod a poor second and daisy faintly positive. Since these plants are related, such findings

are believed by most competent observers to be an example of "group reaction," so familiar to bacteriologists. If this interpretation is the correct one, the reactions caused by goldenrod and daisy are in the majority of instances to be disregarded.

There are a certain number of sensitive cases in which pollens are shown not to be the cause even tho the disease occurs in certain seasons only. Such individuals will react to one or more of the proteins of foods, animal dandruff, hair or feathers, or bacteria. With respect to the last mentioned, attention should be drawn to the point made by Walker, that bacteria may cause symptoms simulating hay-fever in two ways: (1) by a sensitiveness to the bacterial proteins; (2) by virtue of the infection by the micro-organism. The latter element was considered earlier in this paper, in referring to the non-sensitive cases. In all these instances, the seasonal incidence would have to be accounted for by a seasonal exposure to the particular protein concerned. This is readily understood in the case of certain foods and animals, and in the case of bacteria it would seem that infection somewhere in the body at stated seasons of the year would have to precede the appearance of hay-fever symptoms due to a susceptibility to the protein of the organism present. An example of a seasonal hay-fever caused by a food protein is described in the paragraphs discussing methods of diagnosis.

Where the proteins of animal hair, foods, and

bacteria are the causal agents of hay-fever symptoms, the disease is *usually* non-seasonal in type. The total number of cases causes by these proteins is comparatively small, as for some unknown reason the symptoms produced by susceptibility to the substances are nearly always asthmatic in nature. Hay-fever symptoms are fairly frequently found, however, in persons riding horses or fondling pets, such as cats and dogs. Zinsser[6] cites the case of a laboratory attendant who was always seized with violent sneezing attacks, with running of the eyes and nose, whenever he handled guinea-pigs in the course of his work.

Symptoms.—In those who are affected with hay-fever, the disease makes its appearance every year at approximately the same time. It begins as an irritation of the nasal and conjunctival mucous membranes, with itching and sneezing as prominent symptoms. In a very short time, the eyes begin to water profusely, and there is a thin watery discharge from the nose. A cough is sometimes present, and in certain cases, asthma develops sooner or later in the season. There is often marked mental depression, with inability to concentrate the mind. General malaise, headaches and insomnia are sometimes marked symptoms, and in severe cases the disease is of the most distressing character. During the attack the nasal and pharyngeal mucous membrane is rendered so irritable that

[6]Zinsser.—"Infection and Resistance," 1914.

dust or smoke will serve to aggravate the condition produced by the protein to which the patient is sensitive. The symptoms persist until the end of the period of pollination of the particular plant or plants concerned. As pointed out before, the season for the trees is quite short, but the grasses begin early in June and last until late in July. The ragweed season begins about the middle of August and ends with the first heavy frost. Not a few patients are sensitive to both grass and ragweed. In such cases there is little respite from June to October.

Methods of Diagnosis.—The methods employed in the accurate diagnosis of the disease rest on the basis of the observations of Dunbar[7] and others, that in sensitive subjects, the mere placing of the offending pollen upon the slightly abraded skin will cause a local reaction as evidenced by the appearance of the wheal and a surrounding area of erythema. The actual technic as now employed is as follows: A series of very slight scratches with a sharp scalpel are made on the ventral surface of the forearm. These scratches or cuts should not be deep enough to draw blood, and not longer than an eighth of an inch. They should be placed about one inch apart. The one nearest the elbow is left untouched as a control. A small amount of a suspected pollen is placed on the first abrasion, and dissolved by adding a drop of N-100 sodium

[7] Dunbar.—*Zeitschr. f. Immunitatsforsch,* vol. 7, 1907; *Deutsche med. Woch.,* vol. 37, 1911, page 578.

hydroxid. The next scratch is treated similarly with another pollen, and so on down the arm until all the pollens which might reasonably be expected to be capable of causing symptoms at that season of the year, have been applied. In the average case one notices, within a few minutes, a red areola appearing around the abrasions treated with the offending pollens. In the center of this areola, about the scratch, a wheal will be observed which gradually increases in size. The test is considered complete after thirty minutes, but it is usually unnecessary to allow the solutions to act longer than fifteen minutes.

Some observers prefer to inject solutions of the pollen protein intradermally instead of performing the cutaneous test as outlined above, but there are valid objections to this method. Chief among these is the fact that it is often difficult to differentiate a slight positive reaction from a negative one, as the injection of any solution into the skin necessarily gives rise to a wheal of certain proportions, due merely to the bulk of the fluid. Other objections will be considered in taking up the technique of estimating dosage in treatment.

While the diagnosis of hay-fever may usually be made from the symptoms complained of by the patient, there is likely to be, nevertheless, quite an appreciable percentage of error if more accurate methods are not employed. Cases complaining of symptoms simulating seasonal hay-fever may present themselves, and the diagnosis

seem to be so obvious that sensitization tests appear superfluous. Such a case was tested by the writer in the clinic of Dr. I. Chandler Walker at the Peter Bent Brigham Hospital in Boston, and is cited by the latter in his recent paper.[8] This case, a housewife, complained of sneezing, watery secretions from eyes and nose, and general symptoms of coryza during the summer only. The history of her case did not differ materially from that usually obtained from patients sensitive to both the grasses and ragweed. Tests with the pollens, however, were entirely negative, and in subsequent routine tests with animal and food proteins, she was found to be sensitive to the proteins of wheat. We were at a loss to explain the periodicity of her trouble on this basis until she volunteered the information that every summer she takes a position as baker in a summer hotel. Apparently the ingestion throughout the winter of wheat bread and other foods containing wheat flour is not sufficient to produce symptoms, but that added to the amount of wheat protein breathed into the nostrils during the mixing of pastry, etc., pushed her over the threshold.

Treatment. Specific protein treatment.—The most successful method of treating hay-fever has proven to be the prophylactic inoculation of the patient with the specific protein causing the disease. Solutions of the pollen protein are

[8]Walker.—*Jour. Am. Med. Assoc.*, September 18th, 1920.

made, grading the dilutions of the protein from 1-500 to 1-20,000 or higher. A preliminary test with the various dilutions is made by placing a drop of the solution on a scratch on the skin, having as many scratches as there are dilutions of the pollen. The initial dose (hypodermic) of the pollen will be 0·1 c.c., of the dilution next higher than the last one giving a positive skin test. Suppose 1-5000 gives a faintly positive test; the schedule of treatments would then be 1-10·000 give 0·1 c.c., 1-5000 give 0·1 c.c., 0·2 c.c., 0·1 c.c., 1-1000 give 0·1 c.c., 0·2 c.c., 1-500 give 0·1 c.c., 0·2 c.c., 0·3 c.c., 0·4 c.c., 1-100 give 0·1 c.c. and 0·2 c.c. (Walker).

Some workers use the intradermal injection of the various dilutions to determine both the diagnosis and the degree of sensitiveness. Not only does this method produce a slight wheal from the injection itself, but even comparatively inert substances may produce effects which are only with difficulty differentiated from a slightly positive test. For this reason this method is not to be depended upon to determine the initial dose to be administered in the process of desensitization, whereas the cutaneous method lends itself admirably for this purpose.

The treatments should be given one week apart, and should be completed by the time the season begins. *Therefore the course of inoculations should begin three months before the attack is expected.* Such a course of treatment should protect the patient for that season, and

the schedule will have to be repeated each year —at least for a few years.

In cases sensitive to animal hair, a similar routine is carried out over quite a long period until the skin test shows the patient to be no longer sensitive to strong solutions of the protein. The most satisfactory method of treating food cases is simply to omit such food from the diet. Abstinence for a year or more often results in an automatic desensitization of the patient, who may then add the food to the regular diet without ill effect.

Climate.—For those who are able to do so, a sojourn during the hay-fever season in one of the resorts which are free from the offending pollen will usually prove efficacious. Muskoka and the Georgian Bay are free from ragweed, altho some goldenrod is found. Generally, speaking, however, the autumn cases do well in these localities.

8. Frequent Causes and the Treatment of Perennial Hay-Fever*

By Chandler Walker, M.D.

BOSTON

During the last five years while I was studying bronchial asthma, many patients who complained of having hay-fever throughout or at any time of the year presented themselves for study and treatment. All of the patients that are presented in this paper were either examined while under observation or had recently been examined by competent nose and throat specialists in order to exclude pathologic conditions, growths and the like, that might be the cause of symptoms. On some of the patients, repeated nasal operations had been performed; with others, no cause for operation had been found, but much local treatment had been given. Therefore it may be stated that most if not all of these patients had symptoms that were not benefited by the usual treatment employed by rhinologists. As will be shown in this paper, the cause of the symptoms in such cases may often be determined by cutaneous skin tests, and relief

* From the medical clinic of the Peter Bent Brigham Hospital. Reprinted from The Journal of the American Medical Association, Sept. 18, 1920, Vol. 75, pp. 782-789. Copyright, 1920. American Medical Association, Chicago.

may often be obtained by consentient treatment.

Altho it has been well known for years that certain persons have hay-fever from exposure to animals, only recently has the real causative agent been recognized and appropriate treatment instituted. For these reasons it seems worth while to give a few protocols illustrative of these cases. Likewise, since the ingestion of foods and the presence of bacteria in the nasal cavities, exclusive of a definite infectious process, have only recently been recognized as a possible cause of perennial hay-fever, a few protocols illustrating these cases will be presented. The association of hay-fever symptoms throughout the year with true pollen or seasonal hay-fever and with olfactory irritants will be discust. Finally, attention will be called to a group of cases in which there were eye symptoms alone as a result of eating certain foods.

With those patients who have perennial hay-fever due to animal emanations, foods and pollens it is usually the protein in these substances that causes the symptoms; in the case of the bacteria it may be the protein or it may be the infectious element. In testing with the animal emanations or epidermal proteins, the protein and the peptone should be used separately; with the cereal grains, the globulin fraction of the protein is most important; with other foods and with pollens and bacteria the whole protein seems to suffice. Before treatment may be given to those who are sensitive to a protein, cutaneous skin tests should be made with different dilu-

tions of the offending protein, and treatment should be started with the strongest solution that fails to give even the slightest degree of reaction.

Described briefly, the cutaneous skin test consists of inoculating a series of small cuts or scratches on the flexor surface of the forearm with the different proteins to be tested. A positive reaction consists of a definite wheal, with or without an area of erythema, and the protein giving such a reaction is usually the cause of the symptoms and should always be considered as the cause until proved otherwise.

PERENNIAL HAY-FEVER CAUSED BY HORSES

I have successfully treated twenty patients who had hay-fever caused by emanations from horses. Many of the patients knew that exposure to horses caused their symptoms, and they desired to be treated so that they could be around them. Others were not aware of the cause of their symptoms until the cutaneous tests were made. Protocols of ten cases will be given in more or less detail. Protocols of the other ten cases will not be given because they closely resemble those being presented, and they furnish nothing of additional interest. Two of the cases not presented are worthy of mention in that the patients were officers during the recent war, and as such they were required to use horses, which caused them to have violent hay-fever. After several inoculations, however, with the

offending protein these patients were able to be around horses ad libitum without any symptoms.

CASE 1.—L. K. B., a man, aged 31, had had hay-fever caused by horses all his life. The attacks lasted three or four days at a time, and they occurred throughout the year. He was a cashier in a country bank, and whenever, as very frequently it happened in the winter, a person who had been driving a horse shook or brushed his fur coat in the presence of the patient, an attack of sneezing, itching of the eyes and running of the eyes and nose was precipitated by the horsehair and dandruff dislodged by the shaking of the fur coat. The patient also sneezed every morning on arising.

Cutaneous tests were negative with the proteins of the common foods, pollens and feathers, but were positive with the hair of the cat, dog and horse. The patient was most sensitive to the protein of horsehair and dandruff; a dilution of 1 : 100,000 gave a positive reaction.

The patient was treated once a week with a 1 : 1,000,000 solution of horse epidermal protein in gradually increasing amounts; the first dose was 0.1 c.c., and this was increased 0.05 c.c. each succeeding week until 0.8 c.c. was given at one time. During this series of treatments the patient became free from his customary morning sneezing, and the shaking of fur coats laden with horsehair and dandruff no longer caused symptoms; he was still, however, unable to ride behind a horse without having his usual symptoms. Treatment was continued with a stronger solution of

the protein of horsehair and dandruff, namely, 1:100,000, in the same dosage as outlined above, and before treatment with this solution was completed the patient was able to ride behind horses without symptoms.

Case 2.—C. M., a woman, aged 18, for the last four years had been subject to attacks of sneezing, itching of the eyes and running of the eyes and nose and difficulty in breathing through the nose when near horses; these attacks would continue for two or three hours following exposure. She had frequently been awakened by such attacks in the summer time when a horse had passed by the open window of her sleeping room. During one summer which was spent on an island where there were no animals she was free from symptoms, but on returning to the city in the fall she had an attack which lasted two weeks. She was subject to frequent head colds.

Cutaneous tests were negative with the protein of the common foods, pollens and animal emanations, with the exception that the protein of horsehair and dandruff was positive in a dilution of 1:1,000.

The patient was given a series of five treatments at weekly intervals with horsehair dandruff protein in a dilution of 1:10,000, beginning with 0.2 c.c. and increasing the dose 0.1 c.c. each succeeding week. Following these treatments she was able to ride horseback without symptoms, and had very little trouble when riding behind a horse. The patient was then

given a series of twelve treatments with the horse epidermal protein in a 1:1,000 dilution; the first dose was 0.1 c.c., the maximum or last dose was 0.8 c.c., and the increase each time was 0.05 c.c. The larger number of doses in this series was made necessary because several times the patient had a very sore arm following some of the increased amounts, thus necessitating a repetition of the preceding dose before an increase was deemed advisable. During this series of treatments the patient was able to ride behind horses without any symptoms at all, and she had been free from her usual frequent head colds during the last winter. Treatment was then given with a 1:100 dilution of the horse epidermal protein for eight weeks according to the same schedule as outlined above for the 1:1,000 dilution. By this time the cutaneous tests were negative with the 1:100 solution, and the concentrated powder of the hair and dandruff protein gave only a very doubtful reaction, which consisted of a small area of erythema but no wheal. After this the patient was lost sight of for more than two years, when a letter was received from her stating that she was still free from symptoms and was able to be about horses as much as she desired.

Case 3.—W. G. T., a man, aged 29, had had hay-fever symptoms since childhood when he was near horses and when he went into a horse stable; exposure to cold air also provoked hay-fever symptoms. In addition, he had had continuous hay-fever from the latter part of August

to October during the last summer, but never previously.

Cutaneous tests were positive with the protein of ragweed and goldenrod pollens and with the proteins of horsehair and dandruff in a dilution of 1 : 1,000.

Treatment was given with a series of inoculations of the 1 : 10,000 dilution of the epidermal horse protein and then with a series of the 1 : 1,000 dilution as already indicated in Case 2. The patient no longer had symptoms from exposure to horses, nor did exposure to cold air provoke symptoms. The following spring he was successfully inoculated against ragweed pollen hay-fever.

Case 4.—M. W. J., a woman, aged 23, had had hives and sneezing and running of the eyes and nose since infancy when near horses. The hay-fever symptoms occurred at all times of the year and were also caused by dust.

Cutaneous tests were negative with the proteins of foods, pollens, cat hair and feathers. Dog hair protein gave a positive reaction in a dilution of 1 : 100, and both proteins of horsehair and dandruff were positive in a dilution of 1 : 100,000.

The patient was given six treatments at weekly intervals with a 1 : 1,000,000 dilution of horse epidermal protein; the first dose was 0.2 c.c., and this was gradually increased each week until the sixth dose was 0.6 c.c. Following this series of treatments, the patient experienced much less trouble when around horses. Treat-

ment was continued for nine weeks with a 1:100,000 dilution of the protein, and then for nine weeks with a 1:10,000 dilution of the protein; with each dilution the first dose was 0.2 c.c., and each succeeding week the amount was increased 0.05 c.c. By this time the patient had no symptoms whatsoever from horses, and even dust no longer caused symptoms. Seven months have now elapsed since the last series of inoculations, and the patient is still free from symptoms.

CASE 5.—C. S., a girl, aged 10, had had hay-fever when near horses for eight years. She now desired to own and take care of a pony.

Cutaneous tests were positive with the pollens of timothy grass and ragweed, and with both horse epidermal proteins in a dilution of 1:10,000.

Treatment was given with a 1:100,000 dilution of horsehair and dandruff protein six times at weekly intervals; the doses given were 0.1, 0.2, 0.3, 0.5, 0.7 and 0.9 c.c. She was then given 0.2, 0.3 and 0.4 c.c. of a 1:10,000 dilution. Following this treatment she was able to ride behind horses with no sneezing or running of the eyes and nose, altho her eyes would itch and get red. Two more treatments were given with this dilution; then a 1:1,000 dilution of the proteins was given for seven weeks, and finally five treatments with a 1:100 solution were given. By this time cutaneous tests were negative with the epidermal peptone and only slightly positive with the epidermal protein. Treatment

was then begun with the pollens. All of this treatment was given during the winter of 1917. It has now been three years since treatment was discontinued, and the patient has had no symptoms, altho she has owned and taken all the care of a pony and has been around horses freely.

Case 6.—P. H., a girl, aged 8, had had sneezing, running of the eyes and nose and itching of the eyes for several years when riding behind horses. She had had asthmatic attacks since infancy. She had to ride behind a horse to and from school.

Cutaneous tests were positive, along with other proteins, with horse epidermal proteins in a 1:10,000 dilution.

Treatment was given with a 1:100,000 dilution of both horse epidermal proteins until she was able to ride behind horses; altogether, ten treatments were given. After this, horse epidermal protein treatment was discontinued because, since she was now able to ride behind horses to and from school, it was considered best to treat the asthmatic condition which was due to other proteins.

Case 7.—H. B., a man, aged 40, declared that he was so sensitive to horses that he would have hay-fever, followed in a few minutes by asthma, whenever he went on a congested street where there were horses, or whenever he even went into a harness-repairing shop.

Cutaneous tests were positive with the horsehair and dandruff proteins; the peptone was

positive in a 1:10,000 dilution, and the protein was positive in a 1 :1,000,000 dilution.

Treatment was given nine times with a 1:10,-000,000 dilution of the horsehair and dandruff protein at weekly intervals in these doses: 0.1, 0.15, 0.2, 0.25, 0.3, 0.4, 0.5, 0.6 and 0.7 c.c. The patient was now able to go into a harness-repair shop and to go near horses without symptoms. A similar series of treatments was then given with a 1:1,000,000 dilution of the protein, following which circumstances caused an interruption of treatment.

Case 8.—E. G., a girl, aged 13, had had sneezing and running of the eyes and nose and itching of the eyes for the last year when riding behind horses and when on horseback. She desired treatment that she might ride horse-back. She also had hay-fever in August and September.

Cutaneous tests were positive with ragweed pollen and with the horse epidermal proteins in a dilution of 1:1,000.

Treatment was begun with 0.2 c.c. of a 1:10,-000 dilution of both horse epidermal proteins. Three days later the patient rode horseback with others in an enclosed ring which was very dusty, with no nasal or eye symptoms. Treatment has continued with equal success.

Case 9.—M. G., a woman, aged 21, had had hay-fever for ten years; she had a cold in the head all the time; her eyes and nose ran and she sneezed all through the year, and these

symptoms were worse when she was riding behind a horse.

Cutaneous tests were positive only with the proteins of horsehair and dandruff, and with these in a 1:100 dilution.

She was treated nine times with a 1:1,000 dilution of the proteins and five times with a 1:100 dilution. Following this treatment she had no symptoms when riding behind horses, and in general she had much less trouble; still she was not free from symptoms when not near horses. An examination of her nose revealed polyps, hypertrophied middle turbinates, and a very large spur on the septum. Removal of the polyps and spur relieved her symptoms of hay-fever entirely. Therefore, altho treatment with the epidermal proteins relieved the hay-fever, which was caused by horsehair and dandruff, it was necessary to remove the polyps and the spur before complete relief was obtained.

Case 10.—J. C. W., a woman, aged 44, had had hay-fever throughout the year for many years; her symptoms consisted of sneezing and running of the nose and at times stuffing up of the nose for two or three days at a time on an average of once a week.

Cutaneous tests were positive with the proteins of horsehair and dandruff in a 1:10,000 dilution, but were negative with food, pollen and other animal hair proteins.

Treatment was given as outlined in previous cases with a 1:100,000 dilution of the horse epidermal proteins, and then a few treatments

were given with a 1:10,000 dilution, until the patient became free from symptoms. The patient then discontinued treatment for several months until slight symptoms returned; then more treatment was taken for a short time, and again freedom from symptoms resulted. After this the patient went three months without treatment, when slight symptoms again returned, and more treatment was taken, with the usual relief.

The horse protein hay-fever protocols illustrate several points which may well be emphasized. In Cases 1, 2, 5 and 6 the treatment is given in detail in order to show that treatment should be begun with the strongest solution of the protein that fails to give any reaction by the cutaneous test. Each week the amount of the inoculation is slowly and gradually increased until 0.8 c.c. is given as the last or maximum dose before the next stronger solution is given. In Case 2, several doses had to be repeated because some of the amounts caused a sore arm, whereas all of the other patients took the usual schedule of dosage without ill effects. Case 5 illustrates the fact that, if sufficient treatment is given to render the cutaneous test negative with the concentrated powder of the protein, complete and permanent desensitization results since three years have elapsed since the last treatment with no return of symptoms, even tho the patient is constantly exposed to horses. Case 2 probably illustrates this point, since more than two years have elapsed with

equally good results. Case 3 shows that only a very few treatments are required to enable a horse-sensitive patient to ride horseback, and Case 6 shows that a few more additional treatments are required to permit the patient to ride behind a horse. Cases 3 and 4 show that it does not require many treatments to protect a patient from ordinary exposure to horses. Case 10 shows that altho a few treatments will protect a patient for a few months, such protection is not lasting, and more treatment is required after a time. In other words, these protocols show that the longer the course of treatments, the longer and the more complete is the protection, and that sufficient treatment will probably protect indefinitely.

Cases 1 and 7 illustrate the extreme sensitiveness of some persons to horsehair and dandruff proteins, as demonstrated both by their history and by their cutaneous tests. Sufficient horsehair and dandruff protein is carried in the air in congested parts of a city to cause symptoms in patients that are so extremely sensitive to these proteins. The treatment of such patients has to be started with a very dilute solution of the protein, and great care must be exercised in order to avoid an overdose. In spite of these facts, if the cutaneous tests are carefully made, no ill effects result from proper treatment, and satisfactory results are obtained.

PERENNIAL HAY-FEVER CAUSED BY CATS

Cats probably do not cause hay-fever so frequently as do horses, since I have observed only six cases. Four of these patients were willing to dispense with their cats, and after doing so were free from symptoms. Two patients, however, preferred treatment to dispensing with their pet; protocols of these two cases follow.

Case 11.—W. D., a boy, aged 12, once every month had had attacks of sneezing and running of the nose and eyes, followed by wheezing, shortness of breath and cough since 18 months of age.

Cutaneous tests were positive with the epidermal protein of the horse, dog and cat, but the patient was most sensitive to the proteins of cat hair; cat hair peptone gave a positive reaction in a 1 : 10,000 dilution.

Ten treatments were given at weekly intervals with cat hair peptone in a 1 : 100,000 dilution as follows: 0.1, 0.15, 0.2, 0.3, 0.4. 0.5, 0.6, 0.7, 0.8 and 0.9 c.c. Following this a similar series of treatments was given with a 1 : 10,000 dilution. The patient became free from symptoms during the first series of treatments, and he has remained free, altho it has been a year since the last treatment was given, and a year and a half since the last attack.

Case 12.—F. R. J., a woman, aged 23, had had hay-fever throughout the year for fifteen years, and for the last nine years she had known that cats caused her to sneeze, and made her eyes and nose run.

Cutaneous tests were positive with the cat hair protein. She was, however, more sensitive to the peptone. A 1:100,000 dilution gave a positive test.

Six weekly treatments were given with cat hair peptone in a dilution of 1:1,000,000. After this a 1:100,000 dilution was given as follows: 0.1, 0.15, 0.2, 0.25, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8 and 0.9 c.c. During this series of treatments the patient noted slight hay-fever symptoms when she petted a cat. A similar series of treatments was given with a 1:10,000 dilution of the peptone. During this series of treatments she noted that she could fondle cats without any symptoms, and that she had no symptoms when not near cats, as used to be the case. Cutaneous tests were now positive with a 1:1,000 dilution of the peptone, whereas previous to treatment a 1:100,000 dilution gave a positive test.

Naturally, it is easier to avoid cats than horses, and it is preferable to dispense with the offending cat than to take treatment. The protocols show, however, that if it is necessary to desensitize against cat hair, the treatment for cat hay-fever is no different from that for horse hay-fever, and that the results obtained are equally as satisfactory.

PERENNIAL HAY-FEVER CAUSED BY FEATHERS

In testing patients for sensitization to feathers, the protein and the peptone of both chicken and goose feathers should be used. The patient comes in contact with feathers chiefly

through the use of feather pillows, which may contain either or both kinds of feathers. Only two protocols will be given: one illustrating feather pillows and the other illustrating a parrot as well as feather pillows as the cause of symptoms.

Case 13.—S. G., a man, aged 30, had had hay-fever for the last two years, with only one or two days' freedom at any one time. His eyes itched and watered, his nose ran and he sneezed. He also had frequent head colds.

Cutaneous skin tests were positive with both proteins of chicken feathers, but negative with all other proteins.

Since discontinuing the use of feather pillows for the last six months he has been free from symptoms.

Case 14.—R. H., a boy, aged 17, had had sneezing, running of the eyes and nose, and frequent attacks of bronchitis for the last three years, and during the last six months he had had considerable asthma. His nose had been operated on several times without benefit.

Cutaneous tests were positive with the proteins of chicken feathers alone.

On discontinuing the use of feather pillows, his symptoms were greatly improved but not relieved. The patient then mentioned that there was a parrot at his home, and he asked whether this could not cause symptoms. The parrot was then disposed of, and since then he has been entirely free from symptoms.

Altho feather pillows and parrots may

not frequently be the cause of hay-fever symptoms, it is desirable to test with feather proteins and to inquire in regard to the presence of feathered animals at the patient's home. There is no question that feather dust penetrates the coverings of pillows, and for this reason patients who are sensitive to feathers should use a floss pillow.

PERENNIAL HAY-FEVER CAUSED BY OTHER ANIMALS

Altho I have not had cases of hay-fever caused by dogs or by the wearing of furs, such instances probably do occur. Hay-fever among laboratory workers who are around rabbits and guinea-pigs is not rare. I have tested four laboratory workers who had hay-fever; two were sensitive to rabbit hair and two to guinea-pig hair. All four patients were previously exposed to these animals the greater part of each day; but, since avoiding these animals, they have been free from symptoms. For the last two years these patients have had to handle these animals only occasionally, and only when handling the animals do they have symptoms. Inquiry should always be made as to whether there are any pet animals in the patient's home.

PERENNIAL HAY-FEVER CAUSED BY FOODS

It is not uncommon for bakers to have hay-fever symptoms from the inhalation of the cereal grain flours, and it is not rare among housewives. Therefore the cereal grains should

always be tested. Foods that are eaten sometimes cause hay-fever symptoms, but such instances are not so common as are those caused by the inhalation of the proteins. Protocols illustrating interesting cases of hay-fever caused by the inhalation and ingestion of food proteins follow.

Case 15.—M. T., a woman, aged 40, had had nasal trouble all of her life; her symptoms consisted of stoppage and plugging of the nose, thick secretion from the nose, running of the nose, and sneezing. For the last few months these symptoms had become so aggravated that they resembled a perpetual head cold, and consequently no one would employ her in a household.

Cutaneous tests were positive with chicken and goose feather protein and with oat and wheat globulin; all other proteins were negative.

Omission of feather pillows alone relieved her considerably, and omission of oat and wheat from her diet completely relieved her symptoms.

Case 16.—G. C. P., a woman, aged 48, had had sneezing, running of the nose and some itching and watering of the eyes for the last year. During this time she had craved and had eaten raw carrots in quantities.

Cutaneous tests were positive with the protein of raw carrots, but they were negative with cooked carrots and with proteins of all other foods, as well as with those of animal emanations and pollens.

Since she has discontinued eating raw carrots, she has been free from symptoms.

CASE 17.—S. B., a woman, aged 55, had had hay-fever for the last four years; during the winter it was paroxysmal, but during the summer it was constant. After a positive cutaneous test had been obtained, the patient volunteered the information that during the summer she was a baker in a hotel, but during the winter her occupation was housework which required her to bake less frequently; therefore the hay-fever symptoms coincided with her baking.

Cutaneous tests were positive with wheat globulin only.

CASE 18.—G. P. W., a woman, aged 30, had swelling of the eyes, sneezing and running of the nose when she prepared or ate raw celery. She also had hay-fever caused by ragweed pollen.

Cutaneous tests were positive with a protein of celery and ragweed pollen.

CASE 19.—A. W., a woman, aged 52, had had sneezing, running of the nose and eyes, and dulness in her head for seventeen years until she recently learned that these symptoms were caused by eating certain foods, namely, pork, onions, oatmeal and some forms of pastry. Sifting rye flour caused hay-fever, but she had no symptoms from eating it.

Cutaneous tests were positive with the following proteins and none others: barley, oat, wheat, onion, pork and cantaloup.

Since avoiding these foods she has been free from symptoms.

Case 20.—H. M., a woman, aged 37, had had hay-fever or a cold for six years whenever she mixed and baked bread. She had no trouble from eating pastry.

Cutaneous tests were positive with the cereal proteins, namely, rye, rice, barley, corn and wheat. All of the six individual proteins of wheat gave positive reactions.

Omission of cereals from her diet was not sufficient to permit her to bake without symptoms, nor did subcutaneous inoculation with the individual wheat proteins or with the protein of the whole wheat render her immune, altho following this treatment she could bake a little with comparative diminution of her symptoms. However, relief was not sufficient to warrant further treatment, since it was not essential that she continue baking.

Case 21.—W. R. M., a man, aged 47, had had attacks of sneezing and running of the eyes and nose for many years whenever he was exposed to flour dust.

Cutaneous tests were positive with wheat globulin, but were negative with all other proteins.

Several of the cases in the foregoing protocols are worthy of special attention. Case 21 presented symptoms of vasomotor rhinitis for years, and not until cutaneous tests were made was the actual cause determined. In Case 19, symptoms were also due to the ingestion of commonly eaten foods; but the patient was aware of the cause, and cutaneous tests verified the cause. In Cases

16 and 18 there were symptoms only after the eating of less common foods. In Case 17 the cutaneous tests determined the cause of symptons. In Case 20 an attempt was made to desensitize the patient by subcutaneous inoculation so that she might inhale wheat flour without symptoms; this treatment was a failure. In all food sensitization cases it seems advisable to omit the offending protein, and usually this is not difficult to do. Case 21 illustrates a condition which is frequently present in bakers and is not rare among housewives.

PERENNIAL HAY-FEVER CAUSED BY POLLENS

It is not uncommon for seasonal pollen hay-fever patients to have paroxysms of hay-fever and frequent head colds of two or three days' duration throughout the year. The exciting causes of the attack out of pollen season are exposure to dust, sudden changes in the temperature, frosty air, drafts, irritating odors and the like. Following successful treatment for the seasonal pollen hay-fever, these patients usually remain free from symptoms during the ensuing year. It would seem that exposure and sensitization to the pollens had in some way rendered the patients' mucous membranes susceptible to or sensitive to the secondary or minor causes. Therefore, pollens may be a cause of hay-fever outside the pollen season, and such patients may be relieved of perennial hay-fever by successful pollen treatment.

PERENNIAL HAY-FEVER CAUSED BY UNUSUAL PROTEINS

Goodale[1] has observed several cases of hay-fever caused by the inhalation of orris root face powder; these patients gave positive cutaneous tests with both the powder and the crude orris root. I have observed one patient who was sensitive to rice, and the use of face powder containing rice flour caused symptoms. The following protocol of a case that I studied illustrates the fact that perennial hay-fever may be due to the inhalation of any kind of organic substance.

Case 22.—T. G., a man, aged 34, a jewel polisher, had had sneezing, running of the nose, and a stuffy feeling in his head for five years. The symptoms occurred while he was at work, but he was free after leaving his work and whenever he took a vacation from his work. While at work the patient was exposed to considerable boxwood dust, which is very fine and floats in the air.

The patient gave positive cutaneous tests with the protein obtained from the boxwood dust in a dilution of 1:30,000.

After several inoculations with a 1:40,000 dilution of the boxwood protein the patient became free from symptoms while at work. Treatment was continued until the patient was taking a 1:1,000 dilution of the protein, and he continued to be free from symptoms.

[1]Goodale, J. L. Boston M. C. S. J. 175: 181 (Aug. 10) 1916.

PERENNIAL HAY-FEVER CAUSED BY BACTERIA

Twenty patients who had hay-fever symptoms throughout the year caused by bacteria have been studied. Bacteria were considered to be the cause of symptoms for these reasons: The patients were not sensitive to any of the usual proteins to which they were exposed, namely, those of the common foods, animal emanations and pollens. Either repeated examination of the nose and sinuses had revealed no abnormalities, or repeated operations had previously removed and corrected all abnormalities. Finally, many of these patients were either greatly benefited or relieved by autogenous vaccines made from the nasal secretion. This type of case differs from those already discust in this paper in that none of the patients were sensitive to any protein, and eye symptoms were not present. As already noted, all of the previous groups of patients had, in addition to nasal symptoms, itching and running of the eyes, whereas this bacterial group had little or no eye trouble. Therefore, the presence of pronounced eye symptoms indicates probable sensitization to some protein, and absence of eye symptoms indicates the improbability of sensitization to a protein as a cause. It would seem that this group of so-called bacterial cases should more properly be called vasomotor rhinitis rather than hay-fever, in that they differ as already noted from the sensitization cases.

Of the twenty bacterial cases that I studied,

ten were treated by autogenous nasal vaccines with great benefit or relief; five patients who were similarly treated were not benefited at all, and the remaining five were not treated by vaccines but were treated locally by rhinologists without any benefit; the latter five cases serve as controls for those treated with vaccines. It is not my intention to infer that rhinologists, by means of local and operative treatment, fail to benefit or even cure similar cases, because it is well known that the rhinologist does not often fail in such cases. What I do, however, wish to infer is that after all other treatment has failed, autogenous vaccine treatment may result in considerable benefit or even relief; at least vaccine treatment is worthy of a trial as a last resort. Protocols of the ten cases in which treatment with autogenous vaccine gave benefit follow:

Case 23.—S. F. S., a woman, aged 27, had had attacks of "hay-fever" for five years. The attacks consisted of sneezing and running of the nose for fifteen minutes every morning on arising and every evening on retiring.

Cutaneous tests were negative with proteins of foods, pollens and animal emanations.

Treatment was given at weekly intervals with an autogenous vaccine made from the patient's nasal secretion; the vaccine consisted of hemolytic streptococci. The first inoculation was 300 million, and each succeeding week the amount was increased 100 million.

The patient began to improve after the first treatment, and has continued to improve until she became free from symptoms following the seventh treatment.

Case 24.—D. A. H., a woman, aged 18, had had "hay-fever" for several years; she had a head cold most of the time, she sneezed and her nose was irritated and ran.

Cutaneous tests were negative with all of the common proteins.

As in the former case, treatment was given with an autogenous nasal vaccine consisting of a hemolytic streptococcus.

She became free from symptoms and remained free for five months until the cold winter weather set in, when she began to sneeze considerably, although she had no irritation or running of the nose.

Case 25.—F. W. H., a woman, aged 49, had had no hay-fever all through the year for twenty years, but lately she had been worse during the summer. Her eyes itched, her nose ran, she sneezed and her ears itched; these symptoms continued for two or three days at a time with a few days' interval between the attacks.

Cutaneous tests with all the common proteins were negative.

After five treatments, as in the preceding cases, with an autogenous vaccine made from her nasal secretion, she became free from symptoms and remained free without treatment for eight months. The vaccine consisted of *Streptococcus viridans.* The patient then had a return

of the former symptoms, but again she was relieved by similar treatment.

Case 26.—W. D. R., a woman, aged 34, had had hay-fever throughout the year for three years; her eyes ached but did not water, her nose ran, and she sneezed every morning. Dust irritated her nose, and night air irritated so much that her sleep was disturbed.

Cutaneous tests were negative with all proteins.

She was given twelve treatments as in the preceding cases with an autogenous hemolytic streptococcus vaccine made from her nasal secretion. She became very much freer from symptoms, and her nights were entirely free.

Case 27.—I. F., a boy, aged 18, had had "hay-fever" for five years, winter and summer. Each attack might last one day or one week, and consisted of sneezing, running of the nose and eyes, and swelling of the eyes. He had frequent colds in his head and nose.

Cutaneous tests were negative with all proteins.

A culture from the nasal secretion inoculated in dextrose bouillon and on dextrose agar consisted of a pure growth of *Staphylococcus pyogenes-albus.* An autogenous vaccine made from this organism was given at weekly intervals for six weeks; the first dose was 500 million, and this was increased each week by 250 million. The patient became practically free from symptoms and had continued free for eight months when last heard from.

Case 28.—M. F., a girl, aged 14, had had colds in her head like "hay-fever" all the year for as long as she could remember, with the exception that she was free for a period of three or four years following the removal of adenoids.

Cutaneous tests with proteins were negative.

Her nasal secretion planted on dextrose agar grew practically a pure culture of *Staphyloccoccus pyogenes-albus.* At weekly intervals she was given twelve treatments with an autogenous vaccine of this organism in gradually increasing amounts; the first dose was 500 millions, and this was increased each week by 250 million. During this treatment the patient became free from symptoms and still was free when last heard from a year after treatment was discontinued.

Case 29.—O. O., a man, aged 36, had had "hay-fever" for fifteen years; it developed gradually and occurred at all times of the year. The attacks consisted of sneezing, running of the nose, swelling of the nasal mucous membrane and swelling and itching of the eyes. The attacks continued for two or three hours. He also had frequent head colds.

Cutaneous tests were negative with proteins; intradermal tests were somewhat positive with *Staphylococcus pyogenes-albus,* but negative with other bacteria.

Following a series of eight treatments as in the previous case with a vaccine of *Staphylococcus pyogenes-albus,* the attacks became much less violent, and the sneezing and nasal secre-

tion were greatly diminished. A year later the attacks became violent again and the patient requested more treatment. *Staphylococcus pyogenes-albus* vaccine was again given with equally good results.

CASE 30.—H. C., a woman, aged 21, had had almost continuous head colds for three years; her eyes smarted, she sneezed, and she had a watery and sometimes bloody secretion from the nose. Cutaneous tests were negative with all proteins.

Treatment was given a few times with a stock vaccine consisting of *Staphylococcus pyogenes-aureus,* with no benefit. Twelve treatments were then given with an autogenous vaccine of a gram-negative bacillus isolated from the nasal secretion. During treatment with this organism the patient gradually became free from symptoms and remained free for a year after the vaccine was discontinued. She has not been heard from since.

CASE 31.—A. H. L., a woman, aged 38, had had "hay-fever" the year round for many years. She sneezed, her nose filled up, and it felt as if it were stuffed with cotton and then it ran mucus virtually every morning. For the last six years she had not had the sense of smell or taste, and her ears felt as if they were filled up.

Cutaneous tests were negative with all proteins.

An autogenous vaccine consisting of a hemolytic streptococcus was made from the thick

secretion from the nose and nasopharynx and sent to her physician, a nose and throat specialist, who carried out the treatment and later reported that the patient was greatly relieved of symptoms.

CASE 32.—W. C. H., a man, aged 32, had had a watery secretion from the nose and sneezing continuously for a year.

Cutaneous tests were negative with all proteins.

An autogenous vaccine consisting of a hemolytic streptococcus and *Staphylococcus pyogenes-aureus* was made from the patient's nasal secretion. This vaccine was administered by the patient's physician, a nose and throat specialist, who later reported that the patient became free from symptoms.

These cases illustrate the points already mentioned in connection with the bacterial cases. It is noted that in Cases 25 and 29 relapses occurred several months after treatment was stopt, but on resumption of previous treatment both patients again became free from symptoms. In Case 30 the patient was not benefited by a stock vaccine consisting of *Staphylococcus pyogenesaureus,* but was relieved by an autogenous nasal vaccine consisting of a gram-negative bacillus.

OLFACTORY VASOMOTOR RHINITIS, OR PSEUDO-HAY-FEVER

Goodale[2] has called attention to the fact that during pollen seasons certain individuals who are sensitive to and have hay-fever from pollens also have vasomotor symptoms ranging from sneezing to asthmatic attacks due to the fragrance of certain heavily scented flowers that have no pollen or to which pollen the individual is not sensitive. He considers that the symptoms are reflex and that the path of transmission is along the olfactory nerve. The flowers most commonly responsible are lilies, hyacinths, sweet peas and peonies.

It is not infrequent to encounter certain individuals who have symptoms from similar causes at any time of the year. The causes of symptoms may be classified as mechanical, chemical, odorific and thermal. Among the mechanical causes any kind of dust is the most frequent cause, more especially sweeping dust and hay dust; fine powder, such as talcum and the like, is also a frequent cause. Among the chemical irritants, soap powder, lye and ammoniacal fumes are very frequent causes. Among the odorific irritants, heavily scented perfumes, face powders, musty air and stable odors are frequent causes. Thermal irritants concern sudden changes of temperature, as in going from warm

[2]Goodale, J. L. Boston M. & S. J. 175: 181 (Aug. 10) 1916.

air to extreme cold, from moist air to very dry air, and exposure to drafts; a very frequent history is that of a paroxysm of sneezing with or without running of the nose on retiring and on arising. The mechanism seems to be a reflex due to the sudden exposure of the warm and protected skin of the body to cold air, as in getting out of bed and in undressing, during which acts the warm body surface is suddenly and momentarily exposed to cool air; in other words, there is a mild chilling of the body surface. The same mechanism holds for many who take cold easily. Some of these patients are sensitive to some type of protein which may have rendered their nasal mucous membranes sensitive to these irritants; others are not sensitive to proteins. Appropriate protein treatment for those who are sensitive usually relieves these symptoms, no matter what the irritant may be, and occasionally autogenous nasal vaccines will benefit or relieve the non-sensitive individual. Again, it may be well to call attention to the fact that I am dealing with nasal conditions other than those due to abnormalities, growths and the like, which may cause similar symptoms. I am considering only those cases in which no abnormalities other than a possibly congested mucous membrane could be demonstrated or those whose apparent abnormalities had been corrected.

CONJUNCTIVITIS DUE TO FOOD PROTEINS

Conlon[3] reports three cases of conjunctivitis unaccompanied by any other manifestations that were caused by eating certain foods, and the patients gave positive cutaneous tests with the respective protein. One protocol follows:

A. B. R., a man, aged 56, merchant, for the last four or five years, had been unable to read for more than five minutes at a time without, as he exprest it, a feeling of sand in his eyes; the lids felt constantly as they do when one is very sleepy. He had frequent, sudden attacks of lacrimation, which came on without any known cause and stopped as suddenly as they started. He said that he had had a perfectly miserable time of it for the last couple of years, with virtually constant eye discomfort; so he became an ''early to bed and late to rise'' sort of fellow, as the only time he was at all comfortable was when his eyes were closed. His glasses had been changed a number of times, tinted lenses had been ordered and worn, and drops of various kinds and colors had been prescribed and used without any benefit whatsoever. The eyelids were slightly swollen and congested, and there was a general enlargement of the conjunctival blood vessels which was more marked on the bulbar conjunctiva. Nothing was found in the nose or throat. The general condition was good. He had no bad habits, did

[3]Conlon, F. A.: Am. Jour. Ophth. 2: 486 (July) 1919.

not smoke or drink, and no change was found necessary in his glasses.

On a recent skin test with more than thirty proteins, this patient reacted to egg alone.

The elimination of eggs from his diet was shortly followed by a total disappearance of his annoying symptoms. For the last two years he has been able to use his eyes as he wished, and he reports that life is once more worth living. One control test (eating egg) was followed by a return of his symptoms.

Conlon makes the following comments on this group of cases:

The skin test should be made at the time the patient is suffering from the conjunctivitis, as in some people the anaphylactic reaction disappears after the patient abstains from the offending food any length of time, to reappear again on eating it.

In the absence of uncorrected ametropia, all recurring low grade inflammation of the conjunctiva which the patient calls "frequent attacks of red eyes" should be considered as possibly due to food anaphylaxis. This is especially true when the attacks appear the same months year after year. After obtaining a positive skin test, the proof as to this food being the cause of the conjunctivitis is readily obtained by the patient.

Conlon also believes that the study of food protein anaphylaxis and bacterial protein anaphylaxis will explain the etiology of a number of eye diseases, especially keratitis and low

grade inflammations of the uveal tract, and will open up vast and fruitful fields for investigation.

CONCLUSIONS

Perennial hay-fever is frequently caused by animal emanations, and cutaneous tests should be made with the common animal epidermal proteins.

Those patients whose hay-fever is caused by exposure to horses may be successfully treated by repeated inoculation in gradually increasing amounts of the particular epidermal protein to which they are most sensitive.

Those patients who are sensitive to cat hair protein may be treated similarly with equal success. Dispensing with the cat, however, is easier of accomplishment and is usually beneficial.

With those who are sensitive to the epidermal proteins of other animals (pets), it is preferable to avoid that particular animal. Sensitization to feather protein from feather pillows is frequent, and the substitution of floss pillows is desirable.

Perennial hay-fever is frequently caused by the ingestion of foods and by the inhalation of the cereal grain flours. Cutaneous tests often reveal such a cause, and omission of the protein is the desirable mode of treatment.

Patients who have seasonal pollen hay-fever frequently have paroxysmal symptoms throughout the year. Satisfactory preseasonal treatment

with the particular pollen that causes the seasonal hay-fever frequently relieves the perennial symptoms.

Recurring head colds are frequently coincident with the foregoing sensitizations, and relief from these head colds usually follows proper treatment, as already outlined. This type of head cold is probably not due to an infection but rather a result of sensitization which renders the nasal mucous membrane easily irritable.

Non-sensitive patients with perennial hay-fever or vasomotor rhinitis, provided there are no demonstrable abnormalities, growths and the like in the nasal cavities or sinuses, are sometimes benefited or relieved by autogenous vaccines made from the nasal secretion. The same statement also holds true for those patients who are subject to frequent head colds.

Olfactory vasomotor rhinitis, or pseudo-hay-fever, caused by mechanical, thermal, chemical and odorific irritants, is not uncommon and should be recognized.

The ingestion of foods may cause symptoms referable to the eyes alone. Therefore, altho protein sensitization should not be considered as a ''cure all' or a cause of all obscure conditions, the cutaneous test for protein sensitization deserves a place among diagnostic tests; and when properly performed and interpreted, it is a very useful test.

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9. The Calcium Salt Treatment

By Harold Wilson, M.D.[1]

The reports of Emmerich and Loew[2] on the very favorable results secured by them from the prolonged administration of calcium chlorid in the treatment of hay-fever induced me to make some trial of this drug during the season of 1915. A brief report of the results will be given in this communication.

Whether the ingestion of calcium salts has a direct inhibitory action on the proteolytic reactions which appear to be a necessary part of the hay-fever complex, or so modify this reaction as to render the split proteins less toxic, or whether they act by lessening the patient's nerve irritability, seems at this time to be quite undetermined. The employment of calcium salts in hay-fever would be on a much better basis if we were able to rationalize it. At present, it seems to me that this method of treatment can hardly claim to be more than "reasonable empiricism." In view of the fact, however, that much other useful therapy rests

[1] Gouty and rheumatic cases are undoubtedly much benefited by the use of calcium salts as Dr. Wilson points out in this article.

[2] Emmerich and Loew: Erfolgreiche Behandlung des Heufiebers durch lange Zeit fortgesetzte Chlorkalzium-Zuführ, München. med. Wchnschr., 1913, lx, 2676; Wietere Metteilungen über Erfolgreiche Behandlung des Heufiebers, ibid., 1914, lxii, 41.

on a no more secure foundation than this, there is no reason why we should not make a sufficient trial of this method, which has, certainly, many practical advantages.

Twenty-six patients were treated by me during the past season. Of these, twenty-two were treated exclusively with calcium chlorid, and four patients, who had been under treatment by means of injections of pollen solution, were given the drug when their hay-fever symptoms began to develop more or less severely.

One patient had hay-fever of the vernal type only; three patients had both vernal and autumnal attacks, and twenty-two patients had only autumnal attacks. Twenty-two patients gave a positive ophthalmic or cutaneous reaction to ragweed pollen; four gave a negative reaction to ragweed. Many cutaneous tests were made with substances other than pollens, the result of which will be made the subject of another report.

Treatment was begun in June, with seven patients; in July with four; in August with fifteen, and in September with two. In no case did any patient take the drug for more than eight or ten weeks before the time of the expected attack, and in most cases the period was much more brief. Emmerich and Loew advise the use of the drug over a very long period, as much as a year, if possible. Altho it has been shown that the maximum calcium retention in the system occurs only after its prolonged ingestion, it remains to be proved that its optimum

therapeutic effect in hay-fever requires its daily use for a year before the expected attack. In some of the most favorable cases here reported, the relief secured came almost at once, or after taking, at most, only a few doses.

For most patients the calcium chlorid was prescribed thus:

Calcium chlorid crystals	100 gm.
Distilled water to make	500 c.c.

M. SIG.—Take one teaspoonful in sufficient water with or after each meal.

This gives the patient about 3 gm. of calcium chlorid daily. The crystalline salt is used in preference to the anhydrous, as making a cleaner and clearer solution. When the anhydrous salt is prescribed, allowance should be made for the water of crystallization, of which in the crystalline salt there are six molecules ($CaCl_2 + 6 H_2O$):

Calcium chlorid, anhydrous	50 gm.
Distilled water to make	500 c.c.

M. SIG.—Take one teaspoonful in sufficient water with or after each meal.

There was no serious difficulty in taking the drug as thus prescribed. One patient experienced gastric distress until the dose was reduced; another complained of weakness and loss of appetite, and had to use it intermittently in a lessened dose; another thought it caused a diminution in the urinary output, while another thought the flow of urine was increased. It has

not been observed that the daily ingestion of 3 gm. of calcium chlorid has been followed by any marked bodily disturbance. In fact, much larger doses than this can apparently be taken with entire safety. Cow's milk contains 0.198 per cent. calcium monoxid. A pint of milk contains about 0.71 gm. calcium. Three gm. of calcium chlorid crystals contain about 0.55 gm. calcium, so that more lime is taken by the daily use of a pint of milk than in the dosage prescribed above.

The table on page 350 gives the results of the treatment with calcium chlorid in the twenty-six cases under observation.

A few of the most favorable reports are given in greater detail:

Case 23.—Miss M. T., aged 21, had had hay-fever since childhood, beginning in May and lasting until frost. She was sensitive to flowers of all kinds, to dust and to wind. She could not sweep floors without marked discomfort. She had no asthma. Eye and nasal symptoms were most marked. She had been using epinephrin solutions until they now aggrevated the trouble. July 2d there were lacrimation, coryza and sneezing of moderate severity more or less continuously. Ophthalmic and cutaneous reactions to ragweed were negative. Calcium chlorid, 1 gm., three times a day, was prescribed. July 9th, eyes were "wonderfully better"; there were somewhat less sneezing and coryza; the patient was less sensitive to dust and wind. July 20th she was much less uncomfortable than

RESULTS OF TREATMENT WITH CALCIUM CHLORID IN TWENTY-SIX CASES.*

Case No.	Type of Hay-fever	Reaction to Ragweed	Duration of Treatment	Result	Remarks
12	A	+	2-3 weeks	+	Under treatment with injections of pollen solutions for ten weeks previously.
13	A	+	2-3 weeks	+	Previous treatment as in Case 12.
14	A	+	2-3 weeks	+	Previous treatment as in Case 12.
19	A	+	2-3 weeks	+	Previous treatment with injections of pollen solutions seven weeks.
22	A	+	10 weeks	0	
23	A-V	—	13 weeks	+++	Immediate improvement and absolute freedom from all symptoms after July 28.
24	A	+	11 weeks	+++	Multiple sensitization.
25	A	+	13 weeks	+	No symptoms until September 1.
26	A	+	16 weeks	+++	No symptoms until September 25. Then only trifling itching in throat and slight sneezing. No other symptoms.
27	A	+	12 weeks	—	September 25, patient writes, "I was worse than usual."
29	A	+	8 weeks	+++	Only slight symptoms.
30	A	+	3 weeks	+	
31	A	+	9 weeks	+	Multiple sensitization (faint).
32	A	+	4 weeks	+	Multiple sensitization.
33	V	—	9 weeks	++	Immediate relief and practical freedom from all symptoms about half the time.
34	A-V	+	5 weeks	+	Reports moderate relief from symptoms during season.
35	A	+	4 weeks	+	Multiple sensitization.
36	A	+	......	....	No report.
37	A	+	5 weeks	++	Very little hay-fever, even in country.
38	A	+	4 weeks	+	Multiple sensitization.
39	A	+	4 weeks	+	
40	A	+	4 weeks	++	Multiple sensitization.
41	A	+	4 weeks	++	Did not take drug regularly.
42	A	—	5 weeks	+++	Peach reaction positive; stopped eating peaches.
43	A	+	2 weeks	+	Left city early in September.
44	A-V	—	13 weeks	+++	Relief immediate and complete; slight recurrences; took drug very irregularly.

* Explanation of signs: A indicates autumnal; V, vernal; —, symptoms worse than usual; 0, symptoms about the same as usual; +, symptoms less marked than usual; ++, symptoms much less marked than usual; very definite improvement; +++, absolute freedom from symptoms, or only trifling and insignificant ones during season.

usual. On the whole, there was a marked amelioration of symptoms. July 28th there was very great relief. The patient was practically free from all symptoms. "I never was so helped by anything before." August 13th, the patient reported that she had had no hay-fever symptoms whatever since last visit. Relief was absolute. September 6th, absolute freedom from symptoms continued. This relief continued throughout the season.

Case 26.—Miss M. R., aged 25, had had autumnal hay-fever seven or eight years; no asthma. Maternal aunt had had hay-fever since childhood. Ophthalmic and cutaneous reactions to ragweed were positive. June 11th, calcium chlorid was prescribed, 1 gm. three times a day, but owing to some gastric distress which it seemed to cause, the dose was much reduced for several weeks. The full dose, however, was taken later and continued. No hay-fever symptoms were experienced until September 5th, when there was slight sneezing, and itching in the throat. During the rest of the season symptoms were practically absent.

Case 29.—Dr. W. A. K., aged 40, had had autumnal hay-fever for fifteen years, and slight asthma recently. July 7th, calcium chlorid was prescribed, 1 gm. three times a day. Patient reported in October that he had experienced only trifling symptoms at any time during the season.

Case 33.—Miss F. P., aged 43, had had vernal hay-fever, usually beginning about June 1st

and lasting until the end of July. June 12th, she was having about the usual amount of trouble. The ophthalmic reaction to ragweed was negative. Calcium chlorid, 1 gm. three times a day, was prescribed, with much relief, almost at once. She reported, August 25th: "I have been practically free from symptoms about half the time. The rest of the time partly free and partly in trouble. About July 28th took a long railway journey, weather dry and dusty, with no hay-fever symptoms at all."

CASE 42.—F. W., aged 28, had had hay-fever, beginning in August, for several years. Father had hay-fever; no asthma. Ophthalmic and cutaneous reactions to ragweed were negative. Cutaneous and nasal reaction to peaches was positive. Calcium chlorid, 2 gm. three times a day, was prescribed. August 25th, the patient was very comfortable, with scarcely any symptoms. Cutaneous reaction to peaches was negative. The patient had stopt eating peaches. During the rest of the season there were very few hay-fever symptoms.

CASE 44.—Miss C. S., aged 25, had had hay-fever for nine years, beginning in early spring and lasting until the second week in October. She had asthma. Symptoms were marked. June 30th, the hay-fever symptoms were distressing. Ophthalmic and cutaneous reaction to ragweed was negative. Calcium chlorid, 1 gm. three times a day, was prescribed. Patient reported September 25th. The hay-fever symptoms, which were severe, disappeared after the

second dose of the medicine, whereupon she promptly stopt taking it regularly. Afterward she took a long auto journey without symptoms. During the summer she had occasional slight symptoms, which disappeared immediately when she took the medicine. She had been practically free from all hay-fever symptoms ever since beginning to take the drug. She thinks the results are "wonderful." She would probably have taken the drug more regularly if it had not seemed to increase the secretion of urine.

1. Some hay-fever patients taking not less than 3 gm. of calcium chlorid daily, even for a short time, are practically relieved from all hay-fever symptoms.

2. Calcium chlorid may be taken in doses of 3 gm. daily for an indefinite time without any apparent injury.

3. It is not indispensable in all cases for a hay-fever patient to take calcium chlorid over a long period of time in order to secure relief.

4. Calcium salts may be given, even when the nature of the patient's sensitization is not known.

5. The clinical results from the administration of calcium chlorid in cases of hay-fever are such as to warrant its further trial.

10. Surgical Treatment

Surgical treatment of hay-fever is frequently necessary when the patient comes to the physician in the midst of the disease and palliative

measures are not possible. In this case I cauterize the small sensitive areas with a flat electrode at a white heat, and without the use of cocain, as the use of a local anesthetic would make it impossible to find the sensitive spot. It is well to find the sensitive areas with the cold electrode, then turn on the current and bring to a white heat. In this way you can cauterize four or five sensitive areas at one time. Cauterization should not be repeated more frequently than every six or seven days.

Nasal catarrh, nasal polypi, deviation of the septum, as well as sinusitis, should be treated long before the paroxysms. Many authorities, including Ballinger, believe sinusitis *is* hay-fever, and, if this is true, selected cases respond to autogenous vaccine. Ballinger quotes Dr. P. M. Farrington's successful treatment by this method. He injects 50,000,000 bacteria at first treatment, gradually increasing the dose to 100,000,000 at third treatment. The injections should be made every third or fourth day.

11. A Summary of Treatment

To one who has read the outlines of treatment given in this book it will appear that success in the treatment of hay-fever can be reached through several avenues,—through sera, surgical work, local application and internal medicines. Preparedness is the watchword of our country, and prevention is the keynote in the management of hay-fever. I, therefore, believe

that hay-fever can be prevented by removing the stigma of neurotic inheritance and anatomical defects in youth and by observing the rules of the Hay-Fever Prevention Association, as outlined by Dr. Scheppegrell and quoted in this book. The careful study of pollen by Dunbar has advanced the possibility of cure by this means and will eventually bring about a more scientific adjustment of the remedy. At the present time, however, treatment has not been satisfactory. A more extended study may give better results. Dunbar has caused many enthusiastic workers to offer the results of their labors, and I have quoted Dr. H. Hays' experience with auto-serum, which should be more fully tested, and with him, the honest efforts of Dr. Manning, Dr. Alexander, and the earnest disciple of Dunbar, Dr. J. L. Goodale, whose conclusions as follows are the last words on pollen therapy.

"Serobiological methods have shown the phylogenetic relationship of the different plant-orders and -families. The application of these discoveries to the treatment of hay-fever by injection of plant proteids promises to assist in the selection of the specific material required for a given case. Definite reactions are elicited in hay-fever by the pollen of the exciting plant when brought into contact with an abrasion of the skin. The intensity of these manifestations may be sensibly diminished by the repeated *parenteral* administration of the proteids in question. Coincident with the diminution in the skin

reactions, there seems to occur an increased tolerance of the exposed mucous membrane to the pollen the plants employed. *Pollen therapy in hay-fever may be regarded at the present time as a promising method of treatment, but its value and the permanence of its results remain still to be definitely established."*

To secure reasonable success it is important that hay-fever patients should begin their treatment at least three or four weeks before the onset of the attack by the use of sedative solutions; a strict cleansing treatment being applied daily, if possible, to the nasal membrane to inhibit the reflex. This local treatment should continue for several weeks. Many patients are relieved with the use of a weak solution of suprarenal, 1:10,000 in normal salt. Again, the antiseptic alkaline solution, with an equal quantity of water, usually is sufficient; many are made better by the use of a weak Dobell's solution, and this is my choice of a solution. The frequency of a reaction causing congestion has rendered an otherwise valuable remedy undesirable. I, therefore, have better results with *mild* alkaline solutions of Dobell's, or the liquor antisepticus alkalinicus. Again, many cases do well on an ointment of suprarenal in white vaseline. A small quantity placed in the nose will last longer and be more agreeable than the solution. In asthmatic patients the adrenalin chlorid in oil, used as a spray, is quite effective in selected cases. The danger in the use of cocain is too apparent to place it in the

hands of the patient. Its use in office work is even questionable.

Many internal remedies have been used, and, altho failure is frequent, I have found quinin, atropia, strychnin, anti-pyrin, iodids and thyroid among those most frequently prescribed. Quinin is valuable in massive doses, both locally (snuffed up the nostril in powder form) and internally. The unpleasantness of the toxic effect is as great as the hay-fever itself, rendering it an undesirable remedy. The same can be said of antipyrin used internally. It must be given in large doses—seven to eight grains 3 or 4 times daily for an adult. Its action is antispasmodic, and similar in effect to that in whooping cough. It is possible, and I believe this is true in many cases, it may act as an antitoxin to the irritant from the pollen, and in this way be of benefit when there are paroxysmal asthmatic symptoms.

The iodids act well in small doses when the secretion is slight, but most patients are made worse by their use. Thyroid, in one grain doses, t. i. d., will increase the secretion, dilate the internal vessels and thus relieve the nasal congestion. The use of thyroid is usually effective in patients over 50 and when there is gout or rheumatism.

The drugs mentioned above are at best only palliative and in no sense curative. From the report of Emmerich and Leow we can hope to cure the chronic tendency of hay-fever (*Jour. A. M. A.*, Jan. 17, 1915). They report five cases that were broken up and the patients

permanently freed from its grip by continued treatment with calcium chlorid. This paper furnished us with the only positive internal remedy and is worthy of more extended trial.

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